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Volume 19 **February, 1952** Number 2

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	Amounts per 6 oz.† of Average Cooked Meat	Percentages of Recommended Daily Dietary Allowances
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Iron	5.6 mg.	47%
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Niacin	9.5 mg.	79%
Riboflavin	0.44 mg.	24%
Thiamine	0.50 mg.	42%

† 7 oz. of fresh meat, when cooked, weigh approximately 6 oz.

The important nutrients of meat, however, are not limited to those given above, for which the amounts needed for adequate nutrition have been established. Other nutrients provided by meat, but for which daily needs have not yet been established, include other members of the B complex—biotin, choline, folic acid, inositol, pantothenic acid, pyridoxine, and vitamin B_{12}—and many minerals essential in nutrition.

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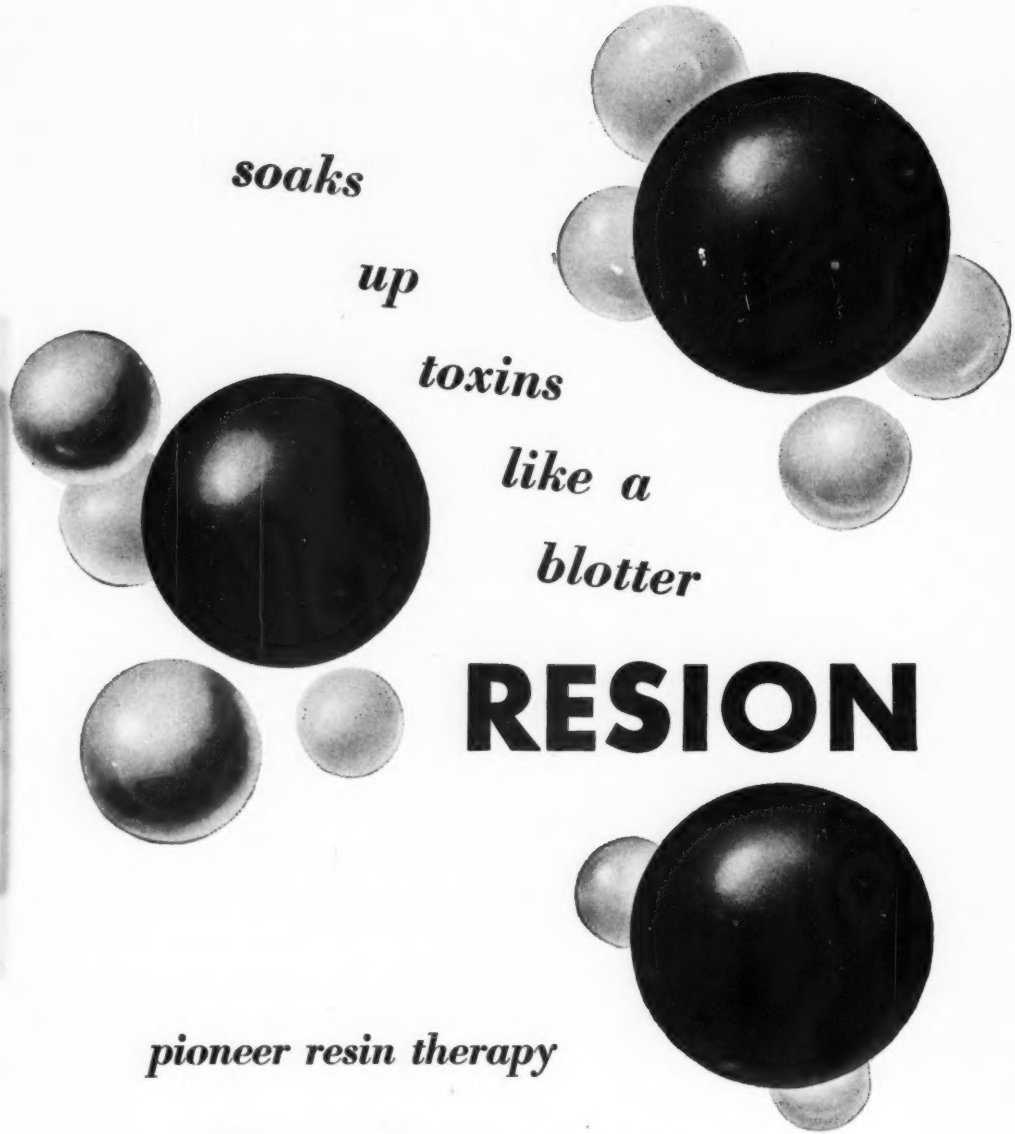
*Watt, B.K., and Merrill, A.L.: Composition of Foods—Raw, Processed, Prepared, Agriculture Handbook No. 8, United States Department of Agriculture, Bureau of Human Nutrition and Home Economics, 1950.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.



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1 Rollins, C. T., to be published.
2 Joslin, C. L.: Del. St. Med. J. **25**:35, 1950.
3 Quintos, F. N.: Philippine J. of Med. **26**:155, 1950.
4 Fitzpatrick, V. P.; Hunter, R. E., and Brambel, C. E.: Am. J. Diges. Dis. **18**:340, 1951.
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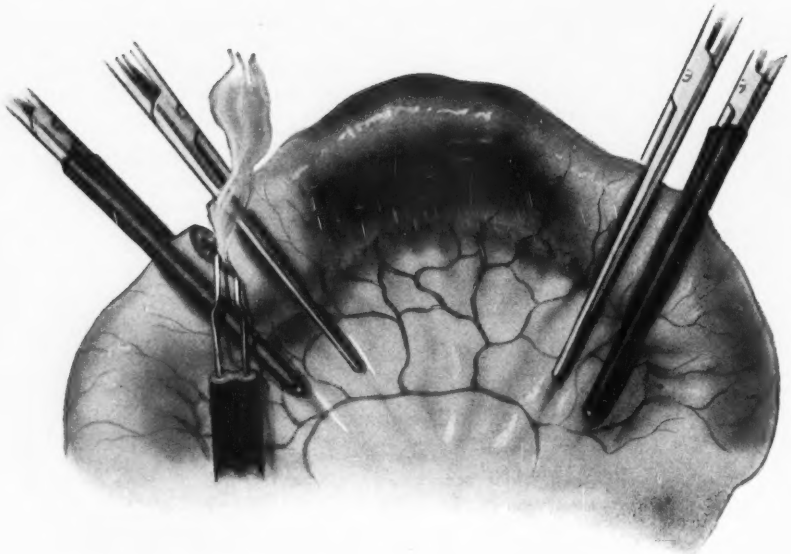

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DiCaprio, J. M., and Ranta, L. A.: Arch. Int. Med. 86:649 (Nov.) 1950.

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CORONARY ARTERIOSCLEROSIS IN DIABETICS

RICHARD W. THALER, M. D. AND CHRISTIAN GEORGE WORNAS, M. D., Boston, Massachusetts.

SERIOUS arteriosclerotic complications develop with unusual and discouraging frequency as the diabetic patient lives longer with his disease. Joslin and Root were among the earliest to stress the important influence of diabetes in the production of arteriosclerosis. It is generally conceded that myocardial infarction increases in frequency proportionately with the duration of diabetes, although there is considerable dispute as to the part played by the severity of diabetes. Root, Bland, and White (1) have shown that diabetics, and especially diabetic women between the ages of 51 and 80 (from postmortem evidence) have much higher incidence of severe myocardial infarcts than nondiabetics. As of the year 1940, it was found that (2a) angina pectoris usually occurred on an average of nine years after the onset of diabetes, and three times as often during the second decade of the disease as during the first decade (2b). Furthermore, 22% more diabetics than non-diabetics die primarily from myocardial infarction (3).

Root and Millard reported in 1948 (4) that in 110 diabetics autopsied at the New England Deaconess Hospital in the period 1940-1946 there was demonstrable coronary arteriosclerosis in 108. When one sees how universal coronary arteriosclerosis is in diabetes of long duration, it becomes apparent that most intensive study of the problem is needed if present efforts to control coronary arteriosclerosis are to be successful.

Bailey (5) feels that four factors favoring the development of arteriosclerotic heart disease are obesity, long duration of diabetes, severity of diabetes, and poor control of diabetes. Hypertension, heredity, abnormal lipid metabolism, sex, age, dietary habits, and possibly smoking are other variables which must be taken into account. It is with the effect of one factor, namely, the careful control of diabetes, on prevention and postponement of angina pectoris and myocardial infarction that this study is concerned.

METHODS

50 diabetic patients from the George F. Baker Clini all with diabetes of ten or more years' duration and all with convincing evidence of angina pectoris and/or myocardial infarction, were selected at random. All patients were living in 1949, at which time a detailed questionnaire was taken, and physical examination, electrocardiograms, and x-rays of the chest were done. Of the 50 patients, 35 were females and 15 were males. All of the patients were 50 to 82 years of age, except one 33 and one 46.

Inasmuch as our patients did not attain the ideal standards of diabetic control, we have established the following more practical criteria as to quality of control:

Submitted August 7, 1951.

New England Deaconess Hospital.

CONTROL OF DIABETES

Good	Fair	Poor
Urine sugar tests:—done properly at least once daily—with urine being kept sugar-free or nearly so (clear green Benedict test).	done at varying and unknown intervals	done rarely with long periods of no testing at all
Blood sugar determinations: at least every 4 to 6 months	occasionally	rarely if ever
Diet: (a) good attempt (as ascertained from answers to careful questions) at carbohydrate restriction	poor or temporary attempts	rarely followed any diet for any length of time
(b) estimated dietary allowances frequently by use of household measures—cups, tsps, etc.	household measures rarely used	never used
or (c) weighed diet at least during early period of instruction as to Rx	did not weigh	did not weigh
Insulin: — taken daily, with amount determined according to urine and/or blood sugar	taken daily in most instances—often without urine or blood sugar checks	not taken or taken sporadically
Regularity of examination by physician: 2 or 3 times a year	approximately once every year or two	only at intervals of many years
Coma:—never	never, or at most once (at time of discovery of diabetes)	0 to one or more times after diabetes diagnosed

A study of the incidence of coronary disease in a group of patients whose diabetes was ideally controlled is urgently needed. It would be very helpful if in the years to come a mass of data on diabetic medical students, nurses, and physicians were collected. It is notable that intelligence and/or the use and application of knowledge about diabetes and diabetic diets played a major part in putting certain of the patients into the *good* category.

According to the previously outlined criteria, 15 patients were classified as having been under good control for the greater part of the duration of their diabetes; 23 could be said to have had poor control. Of our other 12 patients we cannot be sure that their control was "fair" for long enough periods of time to justify any detailed conclusions.

Among the 23 patients who had controlled their diabetes poorly during most of the period since its onset, the following facts were impressive: (1) 8 patients had been in diabetic coma on at least one occasion each. (2) The regularity of a) urine sugar testing at home; b) blood sugar determinations; and c) examinations by a physician was very slight indeed. Each patient gave a history of a period of years (average 11.7, with range 3 to 20) during which time he had been lax and negligent in regard to one or more of the above three important methods of checking up on his

condition. (3) A poor attempt at following the prescribed diet was admitted by all 23 patients. Periods of improper diet habits varied from 5 to 21 years, with an average of 12 years.

In contrast, the 15 patients with good control of their diabetes during the greater part of its duration made a good attempt (as nearly as we could ascertain) at following their diet, save for short periods up to a year in the aggregate. All had made honest efforts at restriction of carbohydrate, and in most cases they measured their food with household measures, for a part of the time—usually at the onset of their diabetes or after discharge from the hospital. Thereafter they judged their diets from what they had learned concerning the caloric values of foods. However, two patients weighed their food for nearly the entire duration of their diabetes. One, now 82 and a patient of Dr. Elliott P. Joslin since 1921, weighed her food every day for 27 years. She also kept a daily 24-hour urine collection and tested a representative specimen from this every day until she developed angina in 1949, at age 81.

Thus, the cooperation of some patients is rewarded. With strong visible and tangible incentives to control diabetes better, more patients can be persuaded to discipline themselves effectively.

Constant instruction and also encouragement of the patient are important, for not only knowledge, but also the ability and determination to apply it, are required for success. Confidence on the part of the physician is necessary. In general, in our series, the patients with "good" control seemed to have a fair degree of understanding concerning diabetes, especially as compared with that found to be possessed by the 23 poorly-controlled diabetics.

Duration of Diabetes: The average duration of diabetes in the entire group of 50 patients was 18.1 years as of December 1949. (One patient died in December, 1949 and two early in 1950) 46 out of the 50 (92%) had a history of obesity at some time in their life. 42 (84%) had had hypertension (either systolic above 140 or diastolic above 90). 10 (67%) of the 15 males and 32 (91.4%) of the 35 females were hypertensive. 5 had been hypertensive before the onset of diabetes. In 26, diabetes definitely preceded hypertension; and in 11 the time of onset of hypertension was not known. Altogether, 45 (90%) developed angina pectoris and 17 (34%) suffered myocardial infarctions.

Among the patients with good control of diabetes, the average age at time of onset of coronary artery disease was 65.6 years. In the 23 with poor control during the greater part of their diabetic life, the average age at the time of onset of coronary artery disease was 56.1 years. This is interesting in view of the fact that the average age, among our whole group of 50 patients, at onset of coronary artery disease was 60.2 years.

Findings: The following table presents data as to duration of diabetes (in the three groups of patients) before the onset of angina pectoris and of myocardial infarction.

From the table it can be seen that the ages of patients in the three groups are comparable, small though the groups admittedly are. Furthermore, it seems that the better-controlled patients live longer with their diabetes before developing cardiac complications secondary to coronary arteriosclerosis than do the poorly controlled patients.

In ten patients with duration of diabetes from 10 through 15 years, poorly controlled, the average age at onset of manifest coronary artery disease was 60.2. In 13 poorly controlled diabetics with diabetes of 16 to 38 years' duration, the average age at onset of manifest coronary artery disease was 53. On the other hand, in 13 patients with "good" control of their diabetes which had been of 16 to 38 years' duration the average age at onset of manifest coronary artery disease was 67.

TABLE I

QUALITY OF CONTROL AND POSTPONEMENT OF CARDIAC COMPLICATIONS IN DIABETES

				Average age at onset of Diabetes Mellitus			Av. No. yrs. Duration of Diab. until onset of coronary artery disease	Average number of yrs. duration of Diabetes Mellitus at onset of				Number of patients with					
		Sex															
Category of Control	Total No. Patients	M	F	Total Group Years	M Years	F Years	By Whole Groups	Angina Pectoris M	Angina Pectoris F	Myocardial Infarction M	Myocardial Infarction F	Angina Pectoris Total	Angina Pectoris M	Angina Pectoris F	Myocardial Infarction Total	Myocardial Infarction M	Myocardial Infarction F
Good	15	5	10	47.9	45.0	49.3	17.7	19.0	18.6	13.3	25	12	3	9	5	3	2
Fair	12	2	10	49.0	48.0	49.2	12.3	12.5	12.3	—	12	12	2	10	3	0	3
Poor	23	8	15	44.2	39.6	46.6	12.0	12.33	11.67	10.5	16.2	21	6	15	9	4	5
Total	50	15	35									45	11	34	17	7	10

The following table gives the age distribution (by decades) of our 50 patients' onset of diabetes and clinical coronary artery disease.

TABLE II

AGE AT ONSET OF DIABETES AND OF CORONARY DISEASE

Age at Onset	No. cases Coronary Artery Disease			No. cases Diabetes Mellitus			No. cases Angina Pectoris		No. cases Myocardial Infarction (with or without angina)	
11-20	0	0%		1	2%		0		0	
21-30	1	2%		3	6%		0		1	
31-40	1	2%		7	14%		1		1	
41-50	4	8%		19	38%		2		2	
51-60	17	34%	88%	18	36%		15	44	5	15
61-70	20	40%		2	4%		19		6	
71-80	6	12%		0	0%		7		2	
81-90	1	2%		0	0%		1		0	
	50			50			45		17	
	88% with onset at 51 or older						44/45 or 97.8% at 41 or older		15/17 or 88.2% at 41 or older	

The average age, for the whole group of 50, at onset of clinical coronary artery disease was 60.2 years.

Among the 15 males the average was 56.4 years; and among the 35 females, 61.8 years.

The average age of the above 45 patients with recognized angina at the time of its onset was 60.7 years. The average age of the above 17 patients at the time of first myocardial infarct was 57.1 years.

For comparison with the above age-at-onset distribution table, the following one prepared by White and Jones (1928) (6) is included.

AGE AT ONSET OF CLINICAL CORONARY HEART DISEASE

0 through 39 years	0.2%
40 through 49 years	6.1%
50 through 59 years	22.7%
60 through 69 years	44.1%
70 years and over	26.9%

Thus, 93.7% of the patients (in a series of 864) had the onset of their disease apparently at the age of 50 or over. (These were not diabetics). Our figures are seen to be in general agreement with this larger series.

Further comparison is offered with other charts of White, Bland and Miskall (1943) (7) and of Bland and White (1936) (8).

Series of 497 patients—1943

Age at onset of Angina Pectoris

0 through 30 years	4	0.8%	
31 through 40 years	16	3.2%	
41 through 50 years	106	21.4%	
51 through 60 years	206	41.4%	
61 through 70 years	131	26.4%	96%
71 through 80 years	34	6.8%	
Over 80	0	0.0%	

Series of 461 patients—1936

Age at onset of clinical coronary thrombosis with myocardial infaretion

0 through 29 years	3	0.7%	
30 through 39 years	16	3.5%	
40 through 49 years	80	17.4%	
50 through 59 years	169	36.6%	
60 through 69 years	142	30.8%	95.9%
70 through 79 years	47	10.2%	
Over 80	4	0.9%	

White (9) states that in this series the average age at onset of angina pectoris was 56.5 years, with an age range of 20 to 80; and that the average age at onset of myocardial infarction was 56.2 years, with a range from 22 to 81. The percentages in our small series are in good general agreement with the above. However, it must be noted that in the above 1936 series of patients with infarctions, 85% were males; whereas only 7/17 or 41.2% of our diabetic patients were males. Likewise, in the above 1928 series of patients with coronary heart disease, 60% were males, whereas only 30% of our diabetic series of 50 are males. This seems to bear out the strong impression that diabetes completely does away with the female's relative "immunity" to severe coronary arteriosclerotic disease. Stearns, Schlesinger and Rudy (11) find that diabetic women over 40 have as high an incidence of coronary arteriosclerosis, angina pectoris and mortality from myocardial infarcts as have diabetic men over 40. E. T. Bell (12) has found, in 1214 diabetic autopsies, that coronary artery disease *caused death* twice as often in male diabetics as in male non-diabetics, and three times as often among diabetic as among non-diabetic females.

SEVERITY OF DIABETES AND INCIDENCE OF CORONARY ARTERY DISEASE

The average total dose of insulin administered at the beginning of its use near the time of onset of diabetes in the 15 patients with good control was 21 units. The average total initial dose among the poorly-controlled patients was 24 units. In 1950, the better-controlled patients were taking an average dose of 39 units daily; and the poorly-controlled patients, 49 units. Among 12 of the poorly-controlled patients who first took 20 units of insulin or less daily, the average age at onset of coronary artery disease was 57.7 years. Among 11 others, also poorly controlled, taking more than 20 units daily at first, the average age at onset of coronary artery disease was 54.4 years. In this connection, it is interesting to note that Stearns, Schlesinger and Rudy (11) in a post mortem study of 643 hearts with coronary arteriosclerosis (54 of which were diabetics') found that the severity of coronary arteriosclerosis was proportional to the duration—but not to the severity of diabetes. This lends further emphasis to the importance of diagnosing diabetes early and then instituting careful control of it.

HEREDITY

35 of the 50 patients knew that there was diabetes in their family. 19 knew of familial coronary artery disease, and 28 (including the 19 above) knew of familial cardiovascular disease of whatsoever form. 21 knew of familial diabetes, but thought there was no familial cardiovascular disease. Among these 21, the average age at onset of coronary

artery disease was 63.7 years. 5 knew of no familial diabetes, but only cardiovascular disease. Among those 5, the average age at onset of coronary artery disease was 54.4 years. 14 patients knew that both conditions were present among members of their families. The average age at onset of coronary artery disease among these 14 patients was 54.6 years. It happened that among the 15 patients with good control of their diabetes, only 4 knew of any incidence of coronary disease in their family, whereas 15 of the 23 poorly controlled patients knew of familial coronary artery disease. 9 of the 50 patients knew of neither any diabetes nor coronary artery disease in their families. These 9 had an average age of 64.3 years at the onset of coronary artery disease. Among the 28 with a known history of familial cardiovascular disease the average age at onset of coronary artery disease was 55.3 years.

The known incidence of familial diabetes both with and without cardiovascular disease, and of familial cardiovascular disease by itself, is significantly higher in our small series than it was in that of Root and Graybiel (10). This fact may be related to our observation of an average age at onset of diabetes somewhat younger than the mean noted by Root and Graybiel.

DISCUSSION

It is noteworthy that the average age at onset of coronary artery disease among our 50 patients is the same as it was in Root and Millard's larger 1946 series (4) of diabetics. At that time there had been an average of 9 years of diabetes before the onset of angina. Even our poorly controlled patients had had diabetes on the average longer than 9 years before developing manifestations of coronary disease. Most of our 12-to-14-year diabetics have had an opportunity to have used protamine insulin most of those years, whereas the long duration patients of 1946 went back to the pre-protamine days of less-prolonged 24-hour control.

The use of low-cholesterol diets has not been a confusing factor in this study. Probably our patients might have had less atherosclerosis and fewer myocardial infarcts if they *had* been on low cholesterol diets, but they were not. It will remain for future investigators to compare the results obtained with good control of blood and urine sugar alone against the results obtained with such control plus the control of dietary cholesterol. In any event, it seems quite likely that a large part of the body and blood cholesterol is formed within the body more or less independent of food intake. Cholesterol determinations, however, do not seem to be the most accurate means of assaying whether or not the process of atherosclerosis is going forward actively at any time. The work of Gofman and his associates (13) seems to indicate that diabetics and patients with marked atherosclerosis, whether or not they show hypercholesterolemia, tend to show consistently a significant serum level of certain low-density, cholesterol bearing lipid and lipoprotein components. These components, the so-called Sf 12-20 group, —which can be detected and quantitated at present by differential ultracentrifugation—are found in much lower concentrations in normal patients without diabetes or atherosclerosis—and in especially low concentrations in young women. Their concentration apparently can be lowered in a high percentage of patients by dietary cholesterol and fat restriction.

In discussing the value of good diabetic control, and the vital importance of following a proper diet consistently, it is well to reemphasize that the diet must be made practical for the patient. It must keep him from being hungry; it must take into consideration his financial means, his place of work, and the amount and type of work he does. His food should not be conspicuously different from that eaten by his friends and associates. His likes and dislikes must be an important factor in the planning of his diet, as must be his and his family's eating habits. One must remember whether or not certain foods that one would like to have the patient eat will be available, and how good the patient's teeth are. If the patient appreciates the physician's efforts to consider all such aspects, he is more likely to cooperate—and thus help himself.

It is difficult to ascertain the true significance of the results presented above because of the influence of various other factors contributing to the development of coronary artery disease. Some of these are 1) heredity (not only for coronary artery disease but also for cardiovascular disease in general and for diabetes); 2) abnormal lipid metabolism; 3) obesity; and 4) hypertension. However, we are convinced that careful control of diabetes helps to keep the diabetic in optimal health for a maximal period of time.

The following tables (14), published by the Metropolitan Life Insurance Company from the experience of the George F. Baker Clinic, demonstrate the value of good control of diabetes (14). A study of 139 patients with onset of diabetes between 15 and 30 years of age indicated that careful management and good cooperation between the diabetic and the physician pay dividends in lowered frequency of retinitis and calcified arteries.

Criteria of Control	Fair control	Poor control
Insulin	Early and continued	Delayed
Diet	Good nutrition	Unregulated
Medical Supervision	Regular	Infrequent
Blood and Urine Tests	Frequent	Rare
Coma	None	One or more attacks

Retinitis

Diabetes of Duration 10-19 years	Diabetes of Duration 20-29 years
Fair control 32% of patients	19% of patients
Poor control 63%	88%

Calcified Arteries

Fair control 62% of patients	76% of patients
Poor control 74%	96%

CONCLUSIONS

How can physicians help to prolong the lives of diabetic patients especially before, but also after the development of coronary artery disease? We recommend the following measures:

1. Good control of diabetes, as judged by our standards. (This involves persistent sincere efforts on the part of both physician and patient).

2. Weight reduction if patient is obese: weight to be kept at normal level or slightly below during entire adult life.

3. Attempts to restrict the ingestion of exogenous cholesterol unless, or until such time as the patient's serum can be shown to contain no abnormal concentration of low-density cholesterol-bearing lipid or lipoprotein components such as are described by Gofman.

4. Early and continuous education of the diabetic.

5. Treatment of the diabetic patient as a whole—the psyche as well as the soma. (This is particularly important because of the deprivations which diabetics must endure.)

6. Efforts to reduce the cost of good diabetic care.

7. Best possible treatment for hypertension whenever its onset.

SUMMARY

1. The fact that coronary artery disease strikes long-duration diabetics, and especially diabetic women, much oftener and harder than non-diabetics is reemphasized.

2. Criteria for calling diabetic control good, fair or poor have been listed.

3. A group of 50 diabetics has been studied in an effort to determine the effect of relatively good diabetic control on prevention or postponement of coronary artery disease.

4. 15 patients whose diabetic control seemed to have been reasonably good had diabetes an average of 17.7 years before the onset of manifest coronary artery disease, and developed coronary artery disease at an average age of 65.6 years. On the other hand, 23 with poor control had their onsets of manifest coronary artery disease after an average of 12.0 years of diabetes, and at an average of 56.2 years.

5. Mildness of diabetes seemed to play less of a part in postponement of coronary artery disease than did good control. It is emphasized that good and prolonged control depends on early detection of diabetes.

6. Close cooperation and understanding between the patient and physician is of vital importance if the patient is to achieve and maintain optimal control of his diabetes. In this series, the patients with the best-controlled diabetes seemed to be those with the most understanding of the disease.

7. Optimal control includes making efforts to (a) consider the diabetic patient as a whole, (b) make his care as economical as is feasible, (c) keep his weight, blood pressure and activities normal; and (d) maintain the patient's proper motivation.

8. It is urged that data relative to the frequency, age, and time of incidence of coronary artery disease in a large group of optimally-controlled diabetics (which should include physicians and nurses and their families) are sorely needed.

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OBESITY, ITS ASSOCIATED DISEASES AND TREATMENT

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INTRODUCTION

IT IS INTERESTING to note that the normal nutritional state commonly called obesity—so well known to all of us, is more or less difficult to define for the purpose of nosography. Bauer (1) aimed at a definition, in which he stated "Obesity is a compulsory tendency toward marked overweight due to abnormal accumulation of fat, by persons who are left alone to their automatic regulations, and are not supervised as far as the intake of food and expenditure of energy is concerned." This definition, it seems to me, offers little that is descriptive of the obese state or its causes. The importance of increased food consumption and proportionally low expenditure of energy are generally admitted by all. The degree to which the endocrine system is involved; by which we mean the thyroid, pituitary adrenals, the gonads and the pancreas, is emphasized by some and minimized by others. The central nervous system has been implicated, inasmuch as it has been noted that injury to the hypothalamus in the experimental animal, incites an inordinate desire for food which is followed by a striking increase in body weight. Recently the relatively older concept of Newburgh (2) and others has been revived. Newburgh emphasized the emotional and unstable personality of certain obese patients who seek relief in the comfort of food when in a state of stress, which may be more or less continuous in such individuals.

Submitted July 14, 1951.

DEFINITION

In the light of what is known today, if I were to define obesity as a clinical entity, I should say that obesity is an abnormal nutritional state characterized by the deposit of excess fat in the subcutaneous and perivisceral tissue. In some individuals there is a distinct hereditary tendency, in others there are evidences of endocrine disturbances, and in a few there are signs of involvement of the central nervous system. In most cases of obesity however, there is a history of excessive ingestion of foods with a relatively low expenditure of energy. The obese state is manifested by abnormal body mass, which sooner or later leads to reduced physical efficiency, physiologic overload, and in due time to pathologic lesions, particularly those of the vascular system, with their usual sequelae. Obesity should be considered as a reversible condition; one that is controllable by restriction of diet and good hygiene.

ETIOLOGY

Before our knowledge on the etiology of obesity can be said to be on a sound basis it will be necessary for us to know more concerning the extent and the processes by which fatty acids are synthesized out of carbohydrate and protein. We should know more than we know now, concerning the part played by the liver in the transformation of fat. We will need to know what impulses govern fat formation and fat deposit in the tissues, and that fat is not a mass of inert tallow laid away under the skin. There are reasons for assuming that all of the body fat makes continuous demands and plays a living part in the daily metabolism. We know that excessive endogenous fat metabolism can induce ketosis, even to the point of coma. That being so, what is there to discount the possibility of a certain daily insulin requirement to ward off a tendency to ketosis of endogenous origin? And, if that were true, does this mean that the diabetic who lives in a state of obesity, carrying 20 to 100 pounds overweight for five to twenty years, is overtaxing his insulin mechanism? In this speculating I am trying to call attention to the complexity of the endogenous and exogenous fat metabolism, and to show that the problem of obesity is not as simple as some of our generally accepted ideas would indicate. One person can build up and break down fat and dispose of it easily; another builds up fat faster than he can break it down, with resulting obesity.

MAXIMUM LONGEVITY TABLES

IDEAL WEIGHTS FOR *MEN*. AGES 25 AND OVER.

HEIGHT (WITH SHOES)		WEIGHT IN POUNDS (AS ORDINARILY DRESSED)		
		SMALL FRAME	MEDIUM FRAME	LARGE FRAME
FEET	INCHES			
5	2	116-125	124-133	131-142
5	3	119-128	127-136	133-144
5	4	122-132	130-140	137-149
5	5	126-136	134-144	141-153
5	6	129-139	137-147	145-157
5	7	133-143	141-151	149-162
5	8	136-147	145-156	153-166
5	9	140-151	149-160	157-170
5	10	144-155	153-164	161-175
5	11	148-159	157-168	165-180
6	0	152-164	161-173	169-185
6	1	157-169	166-178	174-190
6	2	163-175	171-184	179-196
6	3	168-180	176-189	184-202

IDEAL WEIGHTS FOR *WOMEN*. AGES 25 AND OVER.

HEIGHT (WITH SHOES)		WEIGHT IN POUNDS (AS ORDINARILY DRESSED)		
		SMALL FRAME	MEDIUM FRAME	LARGE FRAME
FEET	INCHES			
4	11	104-111	110-118	117-127
5	0	105-113	112-120	119-129
5	1	107-115	114-122	121-131
5	2	110-118	117-125	124-135
5	3	113-121	120-128	127-138
5	4	116-125	124-132	131-142
5	5	119-128	127-135	133-145
5	6	123-132	130-140	138-150
5	7	126-136	134-144	142-154
5	8	129-139	137-147	145-158
5	9	133-143	141-151	149-162
5	10	136-147	145-155	152-166
5	11	139-150	148-158	155-169
6	0	141-153	151-163	160-174

(Metropolitan Life Insurance Co.)

OBESITY AND DIABETES

In our experience, in one series of 2500 diabetics, nearly ninety percent of the cases had a period of marked obesity antedating the onset of the disease. I have known two or three year old children to go through a period of obesity before diabetes made its appearance. It is well known that babies of diabetic mothers tend to weigh eleven pounds or more at birth. Today this is believed to be due to hormonal imbalance in the mother, during the pregnancy. Recently, after delivery of a 12½ pound baby, our obstetrician suggested that the mother be studied for evidence of diabetes. Diabetes was not found then, but four months later, the mother did develop diabetes with marked ketosis. Here the foetus actually revealed the prediabetic state of the mother before the usual clinical methods could detect it. A 12½ pound infant such as this one, is an obese infant, having developed in a milieu of hormonal imbalance.

We know that reducing the weight of a diabetic, increases food tolerance, and lowers insulin requirement; and we also know that a heavy fat diet, even for one day creates the need for more insulin. Further relationship between fat formation and the endocrine system is seen in the fact that insulin favors lipogenesis as well as it increases utilization of carbohydrate and protein.

PATHOLOGY AND PATHOLOGIC PHYSIOLOGY

The lack of a more complete knowledge on the Pathology and Pathologic Physiology of obesity is not so much because the problem has been neglected; rather it is because certain fundamental physiological facts in human metabolism are still unknown. It will be interesting to know 'for sure' what physiologic or pathologic impulses, reflexes and stresses cause persistent hunger and overeating, and why it is that excessive eating, in time, leads to deposit of excess fat in such locations as the abdominal wall, the breasts, the nape of the neck, select areas in certain types of dyspituitarism, and at the girdle area producing the so-called menopausal spread. It will be interesting to learn why and how obesity is induced by certain lesions in the central nervous system.

BACKGROUND OF OBESITY

Every day experience shows that environmental influences, availability and preference for certain foods lead to obesity. Family tendency and personal or

MEN — AGE 25 AND OVER

HEIGHT WITH SHOES		BODY FRAME	IDEAL WEIGHT		CALORIC REQUIREMENT AT 25 CAL./KILO				CALORIC REQUIREMENT AT 27.5 CAL./KILO				CALORIC REQUIREMENT AT 30 CAL./KILO			
Ft.	In.	Build	Lbs.	Kilos	Total per Day	Carb. gms.	Prot. gms.	Fat gms.	Total per Day	Carb. gms.	Prot. gms.	Fat gms.	Total per Day	Carb. gms.	Prot. gms.	Fat gms.
5	2	Small	120	55	1375	130	55	70	1515	150	50	80	1650	170	60	80
5	2	Med.	128	58	1450	150	55	70	1595	160	60	80	1740	180	65	85
5	2	Large	137	62.5	1560	150	60	80	1720	175	65	85	1875	195	70	90
5	3	Small	123	56	1400	140	55	70	1540	150	55	80	1680	175	65	80
5	3	Med.	131	59.5	1485	145	50	80	1635	165	60	80	1785	175	70	90
5	3	Large	138	63	1575	155	60	80	1735	175	65	85	1890	200	70	90
5	4	Small	127	58	1450	150	55	70	1595	160	60	80	1740	180	65	85
5	4	Med.	135	61.5	1540	150	55	80	1690	175	65	80	1845	195	65	90
5	4	Large	143	65	1625	170	55	80	1790	175	70	90	1950	210	75	90
5	5	Small	131	59.5	1485	145	50	80	1635	165	60	80	1785	175	70	90
5	5	Med.	139	63	1575	155	60	80	1735	175	65	85	1890	200	70	90
5	5	Large	147	67	1675	175	65	80	1845	195	65	90	2010	215	85	90
5	6	Small	134	61	1525	155	50	80	1675	175	65	80	1830	195	60	90
5	6	Med.	142	65	1625	170	55	80	1790	175	70	90	1950	210	75	90
5	6	Large	151	69	1725	175	65	85	1900	200	70	90	2070	235	80	90
5	7	Small	138	63	1575	155	60	80	1735	175	65	85	1890	200	70	90
5	7	Med.	146	66.5	1660	175	60	80	1825	190	65	90	1995	215	80	90
5	7	Large	155	70.5	1765	170	70	90	1940	205	75	90	2115	235	80	95
5	8	Small	141	64	1600	165	55	80	1760	170	70	90	1920	205	70	90
5	8	Med.	150	68	1700	180	65	80	1870	195	70	90	2040	210	75	100
5	8	Large	159	72	1800	190	60	90	1980	205	85	90	2160	235	80	100
5	9	Small	146	66.5	1660	175	60	80	1825	185	70	90	1995	205	80	95
5	9	Med.	154	70	1750	180	65	85	1925	205	75	90	2100	230	80	95
5	9	Large	163	74	1850	195	65	90	2035	220	85	90	2220	250	80	100
5	10	Small	150	68	1700	180	65	80	1870	195	70	90	2040	210	75	100
5	10	Med.	158	72	1800	190	60	90	1980	205	85	90	2160	235	80	100
5	10	Large	168	76	1900	200	70	90	2090	220	80	95	2280	255	80	100
5	11	Small	154	70	1750	180	65	85	1925	205	75	90	2100	230	80	95
5	11	Med.	163	74	1850	195	65	90	2035	220	85	90	2220	250	80	100
5	11	Large	173	79	1975	210	80	90	2175	240	80	100	2370	280	85	100
6	0	Small	158	72	1800	190	60	90	1980	205	85	90	2160	235	80	100
6	0	Med.	167	76	1900	200	70	90	2090	230	80	90	2280	265	80	100
6	0	Large	177	80	2010	215	85	90	2215	245	85	100	2400	270	85	110
6	1	Small	163	74	1850	195	65	90	2035	220	85	100	2220	250	80	100
6	1	Med.	172	78	1950	200	75	90	2150	235	80	100	2340	275	85	100
6	1	Large	182	83	2075	230	85	90	2285	260	85	100	2490	285	90	110
6	2	Small	169	77	1925	205	75	90	2115	235	80	95	2310	265	85	100
6	2	Med.	178	81	2025	220	90	90	2230	250	85	100	2430	275	85	110
6	2	Large	188	85.5	2125	235	85	95	2350	280	95	100	2565	280	90	120
6	3	Small	174	79	1975	210	80	90	2175	240	80	100	2370	285	85	100
6	3	Med.	183	83	2075	230	85	90	2285	260	85	100	2490	285	90	110
6	3	Large	193	88	2200	245	80	100	2420	270	85	110	2640	295	95	120

*(Above calculations are in round numbers: disregard slight inaccuracies.)

group habits are of undoubted influence. On the other hand, we all know persons living in such environments who overeat, and do not become obese.

PSYCHIC FACTORS

I have tried to achieve some understanding of the concepts of psychiatrists, and I have been interested in recent studies of obese persons, particularly as they concern occupation, insecurity, nervousness and frustration. Within the limitations of my scant knowledge, I have felt that in some obese patients at least the psychiatrist may read too much into the case. There can be no denying the existence of frustration in certain obese individuals just as there is in certain non-obese ones; but as far as I can see, obesity and frustration are not necessarily fellow travelers. I have seen too many cases of obesity without psychic disturbances, to believe that most of them have psychic backgrounds. Before sending obese patients to the psychiatrist I would also like to know what percentage of cures psychoanalysis has to offer. To suggest that the general run of obese patients consult the psychiatrist, it seems to me, is going much too far. We used to believe that the lean and the hungry were the malcontents; we are now told that the obese are the ones.

There are more than a million diabetics in the United States, of which by our count, 85% to 90% go through a period of striking obesity preceding the clinical onset of the disease. Shall we refer these 850,000 to the psychiatrist? And if not all cases, how shall we do the selecting?

An internist delving into Psychosomatic Medicine, unless he is a very wise man, is in danger of hasty evaluation and premature conclusions; as a result of which he may fall into the arm chair method of diagnosis, slight the importance of the soma and exaggerate the part played by the psyche of the patient. I have seen this happen more than once.

SYMPTOMATOLOGY

In so far as symptoms are concerned is it going too far to say that there really are no characteristic subjective or objective symptoms of obesity, other than one's visual impressions and the register on the scales? Certainly the usual basal metabolism readings have added little to our understanding. As already stated, some obese patients claim to have a contin-

WOMEN — AGE 25 AND OVER

HEIGHT WITH SHOES		BODY FRAME	IDEAL WEIGHT	CALORIC REQUIREMENT AT 25 CAL./KILO				CALORIC REQUIREMENT AT 27.5 CAL./KILO				CALORIC REQUIREMENT AT 30 CAL./KILO			
Ft.	In.	Build	Lbs. Kilos	Total per Day	Carb. gms.	Prot. gms.	Fat gms.	Total per Day	Carb. gms.	Prot. gms.	Fat gms.	Total per Day	Carb. gms.	Prot. gms.	Fat gms.
4	11	Small	108 49	1225	120	50	60	1345	130	50	70	1470	150	50	75
4	11	Med.	114 52	1300	140	50	60	1430	145	55	70	1560	155	55	80
4	11	Large	123 56	1400	140	55	70	1540	150	55	80	1680	175	65	80
5	0	Small	109 49 5	1240	125	50	60	1360	135	50	70	1485	150	50	75
5	0	Med.	116 52 5	1315	145	50	60	1445	150	55	70	1575	155	60	80
5	0	Large	124 56	1400	140	55	70	1540	150	55	80	1680	175	65	80
5	1	Small	111 50 5	1260	130	50	60	1390	140	50	70	1515	145	55	80
5	1	Med.	118 54	1350	130	50	70	1485	150	50	75	1620	170	55	80
5	1	Large	126 57	1425	145	55	70	1570	150	65	80	1710	180	65	80
5	2	Small	114 52	1300	140	50	60	1430	145	55	70	1560	150	60	80
5	2	Med.	121 55	1375	130	55	70	1515	145	55	80	1650	170	60	80
5	2	Large	130 59	1475	150	50	75	1625	170	55	80	1770	170	70	90
5	3	Small	117 53 5	1340	130	50	70	1475	150	50	75	1605	160	60	80
5	3	Med.	124 56	1400	140	55	70	1540	150	55	80	1680	175	65	80
5	3	Large	131 59 5	1485	150	50	75	1635	170	60	80	1785	175	70	90
5	4	Small	120 55	1375	130	55	70	1515	145	55	80	1650	170	60	80
5	4	Med.	128 58	1450	150	55	70	1595	160	60	90	1740	180	65	85
5	4	Large	136 62	1550	150	60	80	1705	180	65	80	1860	195	65	90
5	5	Small	124 56	1400	140	55	70	1540	150	55	80	1680	175	65	80
5	5	Med.	131 59 5	1485	150	50	75	1635	170	60	80	1785	175	70	90
5	5	Large	139 63	1575	155	60	80	1735	180	65	85	1890	200	70	90
5	6	Small	128 58	1450	150	55	70	1595	160	60	80	1740	180	65	85
5	6	Med.	135 61 5	1530	150	55	80	1690	175	65	80	1845	195	65	90
5	6	Large	144 65 5	1640	175	55	80	1800	175	70	90	1695	215	75	90
5	7	Small	131 59 5	1485	150	50	75	1635	170	60	80	1785	175	70	90
5	7	Med.	139 63	1575	155	60	80	1735	180	65	85	1890	200	70	90
5	7	Large	148 67 5	1690	175	65	80	1855	195	65	90	2025	225	80	90
5	8	Small	134 61	1525	150	55	80	1675	175	65	80	1830	195	60	90
5	8	Med.	142 64 5	1610	165	55	80	1775	170	70	90	1935	210	70	90
5	8	Large	152 69	1725	175	65	85	1900	200	70	90	2070	235	80	90
5	9	Small	138 63	1575	155	60	80	1735	180	65	85	1890	200	70	90
5	9	Med.	146 66 5	1660	175	60	80	1825	190	65	90	1995	215	80	90
5	9	Large	156 71	1775	170	70	90	1950	210	75	90	2130	240	80	95
5	10	Small	142 64.5	1610	165	55	80	1775	170	70	90	1935	210	70	90
5	10	Med.	150 68	1700	180	65	80	1870	195	70	90	2040	210	70	100
5	10	Large	159 72 5	1810	190	60	90	1995	215	80	90	2175	235	85	100
5	11	Small	145 66	1650	170	60	80	1815	185	65	90	1980	210	80	90
5	11	Med.	153 69 5	1735	175	65	85	1900	200	70	90	2055	215	80	100
5	11	Large	162 73 5	1835	195	60	90	2020	210	70	100	2205	240	85	100
6	0	Small	147 67	1675	175	65	80	1845	195	65	90	2010	215	85	90
6	0	Med.	157 71 5	1790	175	70	90	1965	215	75	90	2145	225	85	100
6	0	Large	167 76	1900	200	70	90	2090	215	80	100	2280	260	85	100

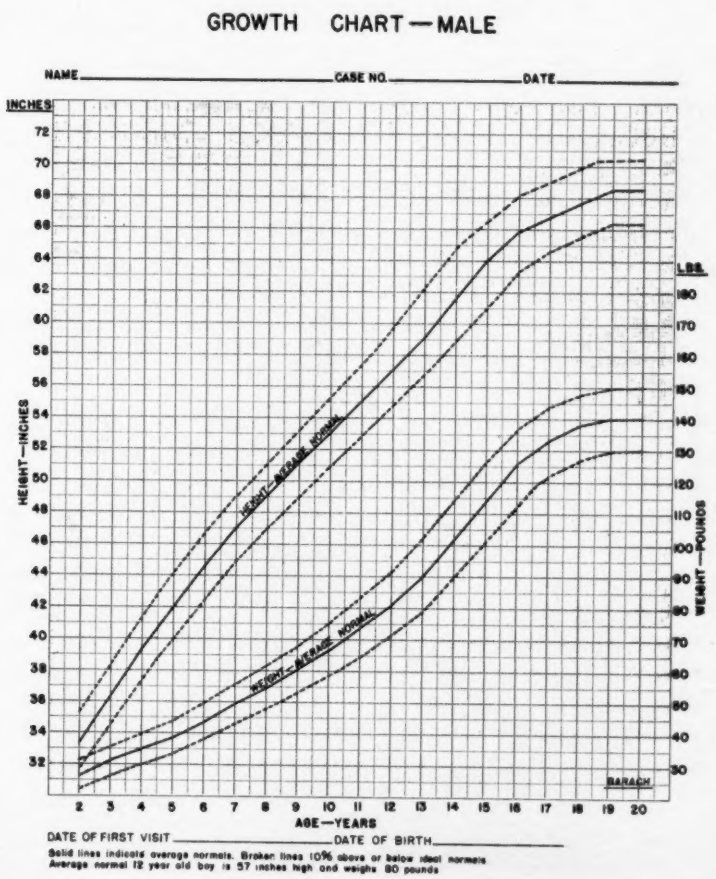
(Above calculations are in round numbers: disregard slight inaccuracies.)

uous craving for food and they eat to satisfy that sense of emptiness.

An interesting explanation of a continuous craving for food might be found in the following assumptions: First, one eats more food than is necessary. This is followed by an increased flow of insulin. If long continued this overabundance of insulin becomes an established state, like the "idea fixe" proposed by Crile, in cases of hyperthyroidism and in cases of hypertension. With this established increase of insulin come symptoms of hyperinsulinism which we know so well. They are restlessness, nervousness, tremor, hunger, faintness, etc. Sooner or later, the patient learns that these symptoms are relieved by more food, which in due time leads to continued overeating, and overweight. Thus a vicious circle is established, and obesity increases. The various stages in this cycle deserve further study and verification.

NORMAL BODY WEIGHT

Up to seven or eight years ago the usual custom was to consider the Actuarial Tables as indices of normal body weight. On reconsideration, however, it was easy to see that these tables revealed only the average weight of a large number of ambulatory persons, and they told little more than that. The average values in the Actuarial Tables include the thin and fat, the young and the old, the well and the sick; and even those on the way to sickness and early death. Since that time, however, we have come into possession of a much better yardstick. Doctors Dublin, Marks, and others of the Metropolitan Life Insurance Company studied the life history of a large group of insurance risks and out of that came the "Maximum Longevity Tables." When all is said and done, the best evidence of optimal health or normalcy is to be found in the total life history of an organism, in its natural environment. In this we assume that the person who lives the longest, is the one who approximates the ideal, in so far as body weight is concerned. It will be noted in the accompanying tables that age, sex, body height and body build, have been included in the calculation. This study revealed the important fact, that those persons who do not at any time there-



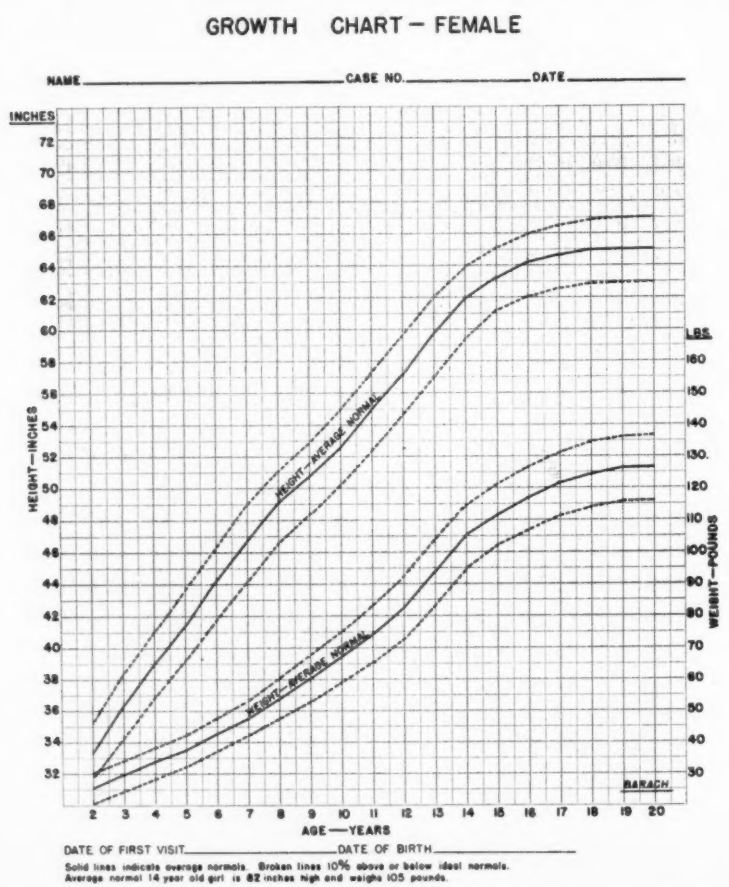
after, exceed the body weight which they attained at the age of 25, are those who attained maximum longevity, the ones who lived the longest.

Since obesity often begins in childhood, I also wish to call your attention to a growth chart based on more than four hundred thousand measurements. This chart portrays what we consider the average normal, for boys and girls of certain height at the succeeding years. It will be noted that a 10% variation above and below the midline is permitted.

Up to the present time, these tables and graphs are the most valuable yardsticks that we know; and we have adopted them to the exclusion of all others.

OBESITY CONTROL

Having decided on the desired body weight for a patient, how do we go about to attain the level of nutrition? The first step in our program is to establish a basal diet for the patient—a diet which will maintain good health and prevent physical deterioration. Such a diet, however low it is at first, must ultimately be close to the basal line, 25 calories per kilo normal body weight. On that basis a woman 5 feet 7 inches tall, medium build should weigh 139 pounds or 63 kilos. At 25 calories per kilo, she would require 1575 calories per day. According to present day practice 1575 calories is too high for a prompt result during the early state of treatment. That being the case, the practical thing to do is to allow approximately three-fourths of that basic diet, until such time as the patient shows a marked reduction in weight, or the need for more food. In our experience the patient's first response to dietetic restriction is always the best. So long as the patient maintains a sense of well being, and cooperates well, this low diet may be continued. When more food is advisable, the diet is increased; but not beyond 25 calories per kilo, ideal body weight, as long as the patient is still overweight. The bad habit of eating to satiety calls for rationalization and re-education of the patient. The use of generous portions of three, six, and nine per cent vegetables and fruits gives the patient a sense of having had plenty of food, yet without excessive nourish-



ment. Certainly this is healthier than destroying the appetite with drugs.

The next step concerns nutrient values of the diet. What proportion of carbohydrate, protein and fat shall enter into the daily menu? Here again we are guided by what we consider physiological. We faced this problem at the beginning of the insulin era (3), 27 years ago, and nothing has occurred since then to invalidate our plan of treatment. Then, as now, we made up our diets to derive approximately two-thirds of the calories from carbohydrate—one-sixth from protein and one-sixth from fats. Thus our patients are supplied with reduction diets that are balanced and in relatively normal proportions. This physiological approach to the problem allows us at all times to feel safe against causing nutritional imbalance. And this, I believe, is better than giving all of one's patients either 800, 1000, 1200 or 1500 calories per day, disregarding the normal ratio of carbohydrate to protein to fat.

In principle, this consists of keeping the diet somewhere between a low and a maintenance level. By doing this we supply enough protein to prevent nitrogen loss or hypoproteinemia, enough fat to meet caloric requirements and plenty of carbohydrate for all the needs of a good maintenance diet. In principle, this plan was used in the survival ration tests for soldiers who lived 11 days on biscuit, vitamin pills, water and salt, and finished with losses up to 30 pounds without apparent ill effects. You will recall the observed fact that these soldiers at first were very hungry, and that after the third day they tore down the pin-up girls with which they decorated the walls of their rooms. That done, they covered the same walls with colored magazine pictures of steaks, fried chicken, salads and other luscious foods. In this behaviour a psychiatrist might have noted how quickly one hunger, the hunger of sex, gave way to another, the hunger for food. The same thing happened as you may recall with those on the "death march" in Bataan, and in the prison camps (4) of the Pacific and in Europe; where hunger was followed by loss of libido and potentia.

I have told some of my recalcitrant patients over the past years that what they really needed for successful weight reduction was three to six months in Poland or Germany or Italy. In those countries, where food has been scarce, a weight reduction of 40 to 50 pounds could almost be guaranteed within several months.

This enforced European experiment with France's 38 million, Italy's 45 million, Germany's 69 million and Poland's 34 million, totalling 186 million people, apparently, is still not sufficiently convincing to some people.—that the way to reduce effectively, is to eat less. Some of our fat ones prefer to experiment with pills and capsules, which may or may not be without harmful side effects and, as previous experience has shown, sooner or later, will be consigned to the trash basket.

As far as I can see there is no compromise on how to reduce body weight. Give maintenance diets; let them be minimal diets, and let them be balanced, and results will follow—as surely as night follows day.

Indoor life favors obesity and outdoor living tends to retard it by increased oxidation and increased dissipation of body heat. Exercise as ordinarily carried out, seldom accomplishes much. To break down a pound of fat requires the dissipation of 4320 calories. Translated into terms of physical activity, this 4320 calories would be used up by a man weighing 145 pounds, in 20 hours of walking during which time he should cover about 60 miles. Sitting and reading, uses up approximately 100 calories per hour, and that would mean no other source of food for 43 hours (5). Lynch (6) suggested that a pound of fat supplies sufficient calories for one to climb to the top of the Washington Monument 48 times.

USE OF DRUGS

As for drugs, Amphetamine (Benzidrine) 15 to 20 mgm. per day is the favorite of many physicians, and especially drug houses. I confess to not using it. It undoubtedly does overcome the desire for food; so will ipecac, and so does a cigarette and a bottle of Coca Cola for breakfast—which I saw a desperate young lady order in a Pullman Diner not long ago. Thyroid extract for reducing has few real indications; and yet how many tons of it has been used in the past? The former enthusiasm for "pituitary soup" injections fortunately is out of date. The one thing that remains, is as it was in the beginning, a low maintenance diet, and determination to attain results, both by the patient and the doctor. Amphetamine, mercurial diuretics and the other drugs have side effects which are not as harmless as some seem to believe. I have seen them do harm, in the presence of organic lesions. Strange to say, the use of simple laxatives, innocent as they are, is hardly ever mentioned in the many learned discussions on the treatment of obesity. I have yet to see harm from them when a suitable one is chosen. The lady who tells her doctor that she is too busy socially and cannot remain home long enough for the laxative to have its effect, had better keep her obesity and toddle along as best she can.

The habit of excessive eating in a way has its counterpart in excessive drinking, and in place of "Alcoholics Anonymous," I would advocate the formation of a society which might well be called "Obesity Invisible." The medical profession has really been helped by the stylists who advocate the slender and the athletic figure of our young women. What still remains for them to do, is to invent a great incentive, to those who do not need, anymore, to "get their man."

SUMMARY

I advocate a hardening of the patient's desire to attain results that are for their good. As a reward for successful weight reduction, or prevention of obesity, we may say to those patients, that by a return to normal body weight, they will delay or prevent the onset of chronic cardiovascular disease such as hypertension and arteriosclerosis in its various forms; certain diseases of the liver and gall bladder, perhaps arthritis, and above all diabetes; and, with these out of the way, they may then look forward to years of more endurable living in the second half of life.

I tell my fat ones that the gates of Heaven are narrow and those who would enter must conform to size.

FAILURES IN THE TREATMENT OF OBESITY

One may well ask, "Why is it that 90% of obese persons, well meaning as they are, fail to achieve the weight reduction which they set out to accomplish?" Mark Twain once said, "To stop smoking is easy, I've done it a thousand times." So it is with the obese, especially women. But, why do they fail?

1. First of all, when it comes to nourishment, we are dealing with a primordial instinct. Every cell in the tissues of a living organism, all day long, cries out for food, and that chorus is loud and resonant. This cellular hunger is something more basic than mere self indulgence or the product of a state of mind, or a lack of will power. In a well balanced organism, physiologic reflexes apprize the individual when he has imbibed sufficient food to meet the metabolic requirements. In a disturbed organism, this control is thrown out of balance, and appetite may be either diminished or increased. The disturbing factor can, of course, be of physiologic or psychic origin. One who sees large numbers of obese patients soon comes to realize that the psychic cases constitute a relatively small proportion of the obese group as a whole. Whatever the modus operandi may be: be it somatic or psychic, one thing is certain, the obese person has ingested more foods than was necessary to maintain normal metabolic requirement. My own experience suggests that there are just as many thin people as there are fat ones who suffer frustration. In fact, if one looks realistically at life, there are few indeed who are free of frustrations of one kind or another. Man is a greedy and insatiable being, and only a few achieve their aims and ultimate objectives, while many reach out unsuccessfully for the same thing. Failure to attain desired ends in the young or the old is the cause of frustration.

2. One of the possible somatic causes of failure to achieve loss of weight in middle age and elderly obese people is, that they lose their normal sense of well being, or they develop a state of physical distress after losing a certain amount of weight. Patients whose loss of girth is striking, not infrequently present well defined evidences of disturbed compensation. They complain of dyspnoea, more marked on exertion, palpitation, tendency to dizziness, early fatigue and asthenia. This is a new experience for them, and they fear it sufficiently to give up diet control and return to their former weight level. My impression of these people is that, over the years they have developed a certain amount of atherosclerosis or arteriosclerosis with loss of the normal elasticity of the cardiovascular system. That with loss of abdominal girth, there is a loss of support for the stiffened abdominal, thoracic and other vessels with alteration in the blood pressure levels. Many patients tell their doctors "you say my blood pressure is better, but I feel worse." This statement is true on both counts. Incidentally, it has long been known that abdominal support restores these patients up to a certain point.

There undoubtedly are other causes of failure in weight reduction, too many to consider here. The physician meeting with difficulty in achieving a restoration of his patients to normal body weight, must not allow himself to become impatient, and at the same time persist cautiously, so long as it can be proved, clinically to be good for the patient.

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EVALUATION OF BLOOD STUDIES IN DIAGNOSIS OF DISEASES OF THE LIVER

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IN RECENT YEARS the diagnosis of liver dysfunction and the differentiation of diseases of the liver and biliary tract have become increasingly accurate. New chemical and biological methods have made it possible to detect deviations from the normal. The proximate or remote relationship of these deviations to the hepatic status remains doubtful in many instances, and since the number of available tests is considerable, one is often faced with discrepancies between them. An attempt is being made in this paper to determine how much diagnostic assistance has been received in a continuous series of 4,926 biochemical analyses performed for the evaluation of liver function.

The data we are presenting concerns the analysis of blood samples only. The exploration of hepatic functional status requires an organized program and includes determination of all the substances excreted through the liver, the use of loading tests, the study of carbohydrate, protein and fat metabolism, the evaluation of the detoxification ability and the estimation of special functions related to the erythrocytes, prothrombin, phosphatases and plasma proteins. Such detailed investigations are carried out in many clinics more or less routinely. The clinical pathologist, however cannot help becoming impressed with the tendency of the physician to initiate his investigation of suspected liver disease by recourse to a group of commonly available analyses of the blood, particularly in cases in which there is no striking single symptom such as jaundice or pain.

Submitted July 19, 1951.

From the Department of Laboratory, U. S. Marine Hospital, Staten Island, N. Y.

In our experience the following nine tests have in the past year become guides in the opinion of the clinicians with whom we are associated to the evaluation of liver disease, particularly as to classification, duration and progress:

Prothrombin	Quick
Cephalin-Cholesterol	Hanger
Thymol Turbidity	Maclagan
Zinc Turbidity	Kunkel
Gamma Flocculation	Huerga & Popper
Bilirubin	Schalm & Schulte
Cholesterol	Sheftel
Alkaline Phosphatase	Bodansky
Albumin-Globulin Ratio	Weichselbaum

We are analyzing the results of testing 810 blood samples, some of which represented repeat examinations, obtained from 415 different patients. The tests listed above were not all performed in every case,

and the total tests 4,926 shows the average number per sample to be slightly over six. The clinician's suspicion of liver dysfunction was confirmed in most cases by one or more abnormal results since only 20% of the samples were entirely negative in all of the tests done on the sample.

We are calling those tests positive in which the following results were obtained:

Prothrombin	75% or less
Cephalin-Flocculation	2 plus
Thymol Turbidity	5 units
Zinc Flocculation	8 units
Gamma Globulin	10 units
Bilirubin	1 mg %
Alkaline Phosphatase	5 Bodansky Units
Cholesterol Total	150 mgs % or 250 mgs %
Cholesterol Esters	60 percent of total
A/G Ratio	1/1

The percentage of positive tests found in the total series was as follows:

Test	*Total*	*% Positive*
Zinc	473	65
Gamma	424	51
Thymol	646	50.5
Cholesterol	441	38.4
Bilirubin	589	31.8
Phosphatase	525	29.8
Prothrombin	572	29.4
Cephalin	657	28.2
A/G Ratio	204	12.2
	4,926	35.8

In an effort to determine whether valuable guidance to clinical conditions is derived from this group of tests, we have analyzed our laboratory results in relationship to the diagnoses finally determined by the combined clinical and laboratory investigation and appearing as the discharge diagnosis on the patients' records. For this purpose we are dividing our patients into two groups: one with normal results in all laboratory tests mentioned; the other with at least one positive test; most of this latter group had several positive tests. Of the 415 cases we were able to follow to discharge and final diagnosis 306.

There were 102 cases showing normal tests exclusively. The diagnoses were distributed as follows:

Alcoholism	10	Diabetes	3
Duodenal Ulcer	8	Gastritis	3
Hepatitis	2	Dermatitis Venenata	3
Metastatic CA	3	Non-thrombopenic Purpura	2
Hypertensive Heart Dis.	4	Infectious Mononucleosis	2
Arterio-Scler. Ht. Dis.	3	Laennec's Cirrhosis	1

The remaining cases, 57% of the total, had a wide variety of systemic, dermatologic, infectious and traumatic states. The total of these cases in which the presence of liver disease may be assumed from the final diagnosis is perhaps too uncertain for even approximate estimation. In our opinion the diagnoses justifying the assumption of liver disease constitute less than 20% of the total.

In the group of cases showing some positive laboratory tests, the diagnoses on discharge are distributed as follows in 204 patients:

Hepatitis	36	Hepatic Disease	8
Laennec's Cirrhosis	16	Hypertensive Heart Dis.	7
Duodenal Ulcer	14	Infectious Mononucleosis	6
Cholelithiasis	14	Syphilis	6
Alcoholism	11	Diabetes	4
Arterioscler. Heart Dis.	8	Pulmonary TB	4
Metastatic CA	8	Hernia	4

The remainder were diversified diagnoses of conditions in which hepatic pathology is not reasonably assumed. One is frequently at a loss to come to a firm decision in regard to the relationship of many of these conditions to the abnormal tests found in them. From the listing it is apparent however that about 50% are cases in which liver disease is diagnosed or may reasonably be expected as a complication. It would therefore seem conservative to state that the presence of even a single positive test of the nine mentioned has considerable correlation with the presence of liver disease in a group of suspected cases.

The relative sensitivity among the nine tests may be expressed by the frequency of positivity of any one test in comparison with the others. This comparison of the relationship of one test to the other has been made by taking each tests' series of positives and tabulating the percentage of this group giving positive reactions with each other test in our battery. In the following listing, Chart I, we have made groups of the individual tests reported as positive in our series. Because of the fact every test was not done in every case; there is a variation in the total number of cases represented in each group. The number following the name of the group gives the total positive tests obtained with the procedure. The percent correlation is indicated for each test.

CHART I

PROTHROMBIN 168		CEPHALIN 218		THYMOL 318	
Zinc	65%	Zinc	78%	Zinc	91%
Cholesterol	48%	Thymol	74%	Gamma	70%
Thymol	48%	Gamma	70%	Bilirubin	44%
Gamma	45%	Phosphatase	53%	Cephalin	41%
Cephalin	44%	Bilirubin	50%	Phosphatase	40%
Bilirubin	42%	Prothrombin	42%	Cholesterol	38%
A/G Ratio	32%	Cholesterol	39%	Prothrombin	34%
Phosphatase	30%	A/G Ratio	27%	A/G Ratio	19%
ZINC 306		**GAMMA 216**		**BILIRUBIN 188**	
Thymol	72%	Zinc	92%	Thymol	68%
Gamma	53%	Thymol	83%	Zinc	67%
Cephalin	51%	Phosphatase	42%	Phosphatase	53%
Phosphatase	44%	Cephalin	39%	Cephalin	38%
Bilirubin	40%	Bilirubin	36%	Cholesterol	37%
Cholesterol	40%	Cholesterol	35%	Gamma	36%
Prothrombin	25%	Prothrombin	26%	Prothrombin	36%
A/G Ratio	20%	A/G Ratio	23%	A/G Ratio	8%
PHOSPHATASE 154		**CHOLESTEROL 158**		**A/G RATIO 37**	
Zinc	74%	Zinc	62%	Zinc	92%
Thymol	65%	Thymol	53%	Gamma	92%
Bilirubin	56%	Phosphatase	47%	Thymol	80%
Cholesterol	56%	Gamma	43%	Cephalin	68%
Gamma	50%	Cephalin	37%	Phosphatase	59%
Cephalin	42%	Bilirubin	35%	Bilirubin	65%
Prothrombin	36%	Prothrombin	31%	Prothrombin	54%
A/G Ratio	18%	A/G Ratio	15%	Cholesterol	43%

RELATION OF TEST POSITIVITY TO LIVER PATHOLOGY:

A summation of the total occurrence of positive results on the several tests is depicted graphically in Figure 1.

When the same analysis is made of those cases clinically diagnosed as hepatitis the relationship of one test to the other is markedly altered. One observes high frequency of thymol turbidity exceeding 1 mg. percent with low frequency of abnormal albumin-globulin ratio. See Figure 2.

In the cases diagnosed as Laennec's cirrhosis, the frequency of positive tests is noted to be high in many more items, with a noteworthy increased sensitivity of the gamma globulin test. Pathological alterations of prothrombin and A/G ratio are seen in higher incidence. The esterification of cholesterol is rarely affected. Alterations of bilirubin are less frequent in cirrhosis than in the hepatitis group. See Figure 3.

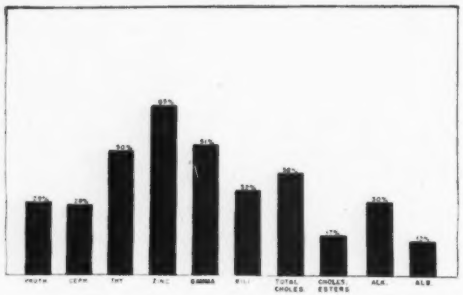

FIG. 1 PERCENT POSITIVE TESTS WITH RANDOM DIAGNOSES.

DISCUSSION

It is apparent that no analysis of the above data can lead to any firm conclusion with regard to the effectiveness of utilizing this group of liver function tests in different diagnosis. Our series of cases was not selected with this type of work in mind. What we hope to accomplish is to determine which among the liver function tests mentioned is most closely correlated with actual disease of the liver, as far as we can determine that such conditions existed from the subsequent history of our patients. In addition we are attempting to reach an opinion concerning the relative merits of the several flocculation tests and the determination of alkaline phosphatase, albumin-globulin ratio, prothrombin time, blood bilirubin and cholesterol.

An interesting and informative account of their experience with the detection of liver cell damage by functional testing was written by Popper, Steigmann and Szanto (10). By a combination of function tests and liver biopsy, these authors determined that the greatest correlation between liver cell damage and positive test existed in regard to cephalin flocculation, thymol turbidity, blood bilirubin, albumin/globulin ratio and alkaline phosphatase. No correlation was found between liver cell damage and prothrombin time percentage or serum cholesterol. In the absence of intrahepatic infection, obstruction of the large bile ducts does not result in positive flocculation tests, and this observation has been made the basis for the belief that these tests are particularly valuable in the differential diagnosis between surgical and medical types of jaundice.

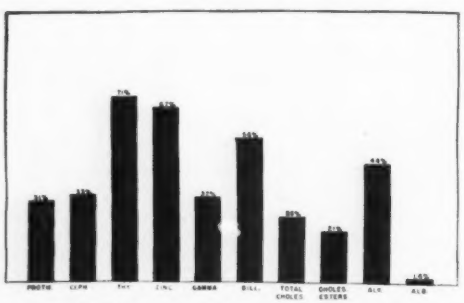

FIG. 2 PERCENT POSITIVE TESTS WITH HEPATITIS AS DIAGNOSIS.

We must be satisfied with a substantial statistical correlation between abnormal hepatic tests and clinical liver disease, even if in individual cases, this correlation is not found. Because of a large functional reserve of the liver, and its great regenerative ability, the physiological status is subject to rather abrupt changes, especially since many of the dysfunctions are closely correlated to change in effective blood supply, (particularly in cirrhosis). In all of our tests of the liver, we are dealing with a combination of factors rather than a basic measurement of a characteristic chemical operation in which the liver alone is active. Probably the only test now available which utilizes a clear-cut hepatic function is the prothrombin response to Vitamin K administration. In our hands we have found that this particular technic is not valuable because many cases of advanced liver cell damage still have normal prothrombin time; that is, the functional capacity of the liver is very great with regard to this particular element.

It is intriguing to speculate about the relationship of the serum protein partition to the appearance of positive flocculation tests. In our series it is noteworthy that positive zinc flocculation and increased gamma globulin were almost invariable whenever the albumin/globulin ratio was found disturbed; either reversed or approaching the 1-1 level. In addition these tests were often positive when the A/G ratio was normal. Electrophoretic studies of the serum proteins have demonstrated abnormal partition and components in a considerable group of cases of acute hepatitis and cirrhosis of the liver reported by Rafsky et al. In many of their cases these changes were not detected by chemical determination of albumin and globulin. On the other hand, their thymol and cephalin flocculation tests were almost invariably positive in the presence of abnormal electrophoretic patterns, and in some instances were positive in the follow-up observations when the electrophoretic pattern was normal.

It appears that the flocculation tests depend upon several mechanisms. In the first place flocculation may result from an increase in gamma globulin; secondly from a decrease in the serum albumin; thirdly, from an increase in lipids associated with beta globulin in lipo-protein complexes; and fourthly, from some change in the property of the serum albumin which inhibits flocculation. (Hanger;—Watson and Rappaport). Some of these flocculation tests are more dependent on one of these mechanisms, some on others. One is led to the belief from our statistics that increase in gamma globulin is rather strikingly associated with cirrhosis of the liver, whereas in acute hepatocellular damage, one finds that those tests dependent on factors other than simple increase in gamma globulin, such as thymol turbidity and zinc flocculation tests, are relatively more sensitive. It is also noteworthy that the reversal of the A/G ratio is only found in high percentage in conditions tending to be chronic. There are relatively few abnormal A/G ratios in acute hepatitis

in our series. The general impression one obtains from this survey is that the various flocculation tests are of considerable assistance in detecting abnormalities of the liver function with the cephalin flocculation rating as the least sensitive. By themselves, however, they do not constitute a means of differential diagnosis, since they measure remote effects of liver dysfunction and there are other conditions which may result in the appearance of abnormal proportions of serum proteins. Thus we have instances in our laboratory of cases of multiple myeloma and kala-azar with the appearance of positive flocculation tests and increase in gamma globulin.

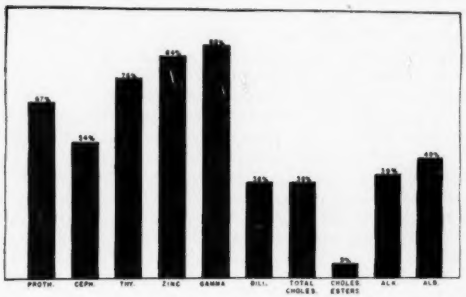

FIG 3. PERCENT POSITIVE TESTS WITH LAENNEC'S AS DIAGNOSIS

It is apparent from Greene's studies that the blood bilirubin level and the alkaline phosphatase of the serum are a measure of biliary obstruction whether extra-hepatic or intra-hepatic and elevated values are observed in portal cirrhosis and in metastatic carcinoma. It is therefore not surprising that these tests, blood bilirubin and alkaline phosphatase, were often found positive in the total unselected series in which the only clinical criterion was suspicion of disease of the liver. Among these cases the presenting finding usually was jaundice and the purpose of the biochemical testing was the detection of hepatocellular damage.

CONCLUSION

1. A survey has been made of a large series of cases in which the clinical status of the liver was evaluated by the determination of the prothrombin time, A/G ratio, the cephalin and zinc flocculation tests, the thymol turbidity test, the gamma globulin content, the blood bilirubin, the blood cholesterol and the alkaline phosphatase.

2. The cephalin flocculation test was found to be the least sensitive of the flocculation tests. In general the flocculation tests were very effective in detecting dysfunction of the liver cells and correlated closely with disturbance of the albumin/globulin ratio when this was present.

3. Elevated bilirubin and alkaline phosphatase were frequently found together.

4. The least valuable tests in this series were the A/G ratio and the determination of the serum cholesterol, both total and esterified.

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ADENOMAS OF THE RECTUM AND THE SIGMOID IN ALCOHOLICS: A SIGMOIDOSCOPIC STUDY

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SINCE 1946 EVERY patient admitted to the Camarillo State Hospital for mental diseases at Camarillo, California has received a complete proctologic examination shortly after entrance. This has been done primarily for the prevention of a possible outbreak of bacillary or amoebic dysentery.

In the course of these sigmoidoscopic examinations adenomata were quite frequently observed and gradually the impression developed that these tumors were more common in a group of patients who not only

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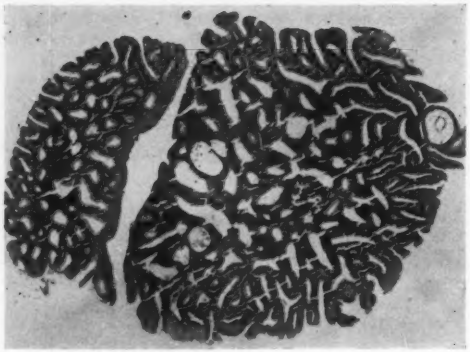

Fig. 1: Adenoma of the rectum with marked proliferative activity. A pre-malignant lesion.

cooperated very well during the examination but also conducted themselves as average individuals rather than as the usual mental patients do. Upon inquiry I learned that those patients were alcoholics, both frequent excessive drinkers and compulsive continuous drinkers.

The problem then presented itself: were adenomas of the rectum and the sigmoid actually more common among alcoholics than among non-alcoholics? The literature as far as it could be traced, failed to throw any light on this subject. My own findings were, to say the least, quite surprising.

Soon after the study was started it became apparent that, grossly, the mucosa of the rectum and the sigmoid in alcoholics was as normal as that in non-alcoholics. It was thin, pale pink in color, freely movable and transparent, clearly revealing the submucosal vessels. In both, the mucosal response to irritants as figs, prunes, laxatives and enemas, and to acute gastro-intestinal infections was the same. Similarly, in both, hypertrophied submucosal lymph follicles, submucous cysts and adenomas were identifiable.

From August 1946 to January 1951 a total of 5,980 patients were sigmoidoscoped. Three hundred and forty-eight of these patients (Table 1) had adenomas, an incidence of 6.81 per cent. Of the total 5,980 patients, 5,160 were non-alcoholic and 820 were confirmed alcoholics.

Among the 5,160 non-alcoholic patients 210 had adenomas, an incidence of 4.07 percent. In this group there were 2,634 females, 89 of whom had adenomas, an incidence of 3.37 percent and 2,526 males, 121 with adenomas, an incidence of 5.46 percent.

Amongst the total 820 alcoholics, 138 had adenomas, an incidence of 16.82 percent. There were 173 females, 20 with adenomas, an incidence of 11.56 percent and 647 males, 118 with adenomas, an incidence of 18.23 percent.

Therefore, adenomas of the rectum are 4.10 times as common in alcoholics as in non-alcoholics, being 3.43 times as frequent in the female alcoholic and 3.34 times as frequent in the male alcoholic. Thus while we can expect to find adenomas in one of every 30 non-alcoholic females and in one of every 18 non-alcoholic

TABLE I

INCIDENCE OF ADENOMA OF THE RECTUM AND THE SIGMOID SIGMOIDOSCOPIC FINDINGS

		Non-Alcoholic			Alcoholic		
	Total	Total	Female	Male	Total	Female	Male
Patients	5980	5160	2634	2526	820	173	647
Adenomas	348	210	89	121	138	20	118
Percentage	6.81	4.07	3.37	5.46	16.82	11.56	18.23
Ratio		1	1	1	4.10	3.43	3.34
Incidence		1 in 25	1 in 30	1 in 18	1 in 6	1 in 8.6	1 in 5.4

males, we should find adenomas in one of every 8.6 alcoholic females and one of every 5.4 alcoholic males.

The age incidence is interesting. From Table II it is seen in the non-alcoholics that each age group is well represented, while in the alcoholics practically all the patients were between 30 and 59 years of age—95 percent of the females and 91 percent of the males. This probably corresponds to the years of heaviest drinking. One (5 per cent) of the alcoholic females was over 59 years of age and of the remaining 9 per cent of the alcoholic males 1 per cent was younger than 30 years and 8 percent were older than 59 years. The youngest non-alcoholic female was 10 years; male, 11 years. The youngest alcoholic female was 30 years; male, 26 years. The oldest non-alcoholic female was 75 years; male, 84 years and the oldest alcoholic female was 63 years; male, 65 years.

In the majority of instances the number of adenomas in each patient (Table III) was limited to one. The numerical incidence of the number of the adenomata in each patient shows little if any difference between non-alcoholic and the alcoholic (Table III). The 100 per cent occurrence of single adenomata among the female alcoholic is too small a series for any statistical significance.

In Table IV the adenomas are tabulated according to their size and to the sex of the patient. From this chart it is seen that the findings are very similar in the 2 groups, the non-alcoholic and the alcoholic. In both, the incidence in the various size groups parallel each other, in both, the 5 mm. to 9 mm. group is the largest one (45 per cent to 55 per cent), in both the large majority of the adenomas (74 per cent to 85 per cent) were under 1 cm. in diameter and in both, the incidence in relation to sex is very similar.

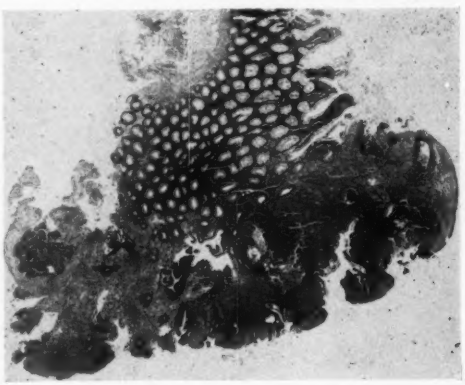

Fig. 2: Adenocarcinoma of the rectum.

TABLE II

AGE INCIDENCE

	Non-Alcoholic				Alcoholic			
	Female		Male		Female		Male	
Age	Number	(%)	Number	(%)	Number	(%)	Number	(%)
10-29	16	(18)	27	(22)	0	0	1	(1)
30-39	23	(26)	22	(19)	4	(20)	27	(22)
40-49	28	(30)	31	(25)	13	(65)	57	(48)
50-59	11	(13)	22	(19)	2	(10)	25	(21)
60+	11	(13)	19	(15)	1	(5)	8	(8)
Total	89	(100)	121	(100)	20	(100)	118	(100)
Youngest	10 yrs.		11 yrs.		30 yrs.		26 yrs.	
Oldest	75 yrs.		84 yrs.		63 yrs.		65 yrs.	

It is evident from Table III and IV that adenomas, whether in non-alcoholics or in alcoholics, once they appear, follow a very similar pattern of development.

DISCUSSION

In the light of the presented data there is an evident preponderance of the incidence of adenomata among the alcoholics as compared with the non-alcoholic. The cause for this high incidence is unknown. The following may be offered for hypothetical consideration as possible causative factors.

There is a consensus of opinion that a reciprocal physiologic relationship exists between the stomach and the intestinal portions of the alimentary tract. For example there is some evidence that the intrinsic factor of Castle which is secreted in the stomach is also produced by the entire gastrointestinal tract, colon included, being synthesized in the argentaffine cells (1). If this be true, it can be assumed, under normal conditions, that the entire gastro-intestinal tract is concerned in maintaining the intrinsic factor at the optimun concentration. Presumably, also, the small and large bowel take over the entire production of this factor when production in the stomach ceases. This might account for the failure of pernicious anemia to be an inevitable consequence of total gastrectomy in man.

The chronic atrophic gastritis seen in pernicious anemia is marked and extensive (Schindler) (2), yet there is evidence that small, inadequate amounts of the intrinsic factor can be secreted by foci of cells in the gastric mucosa which have partially or completely escaped destruction. Perhaps these cells attempting to increase their production of the intrinsic factor undergo hyperplasia and neoplasia.

Supporting this conception are the reports of Velde (3), Rigler and Kaplan (4), Ungley (5), and Schindler (2) which show the great frequency of adenoma of the stomach in pernicious anemia, and those of Kaplan and Rigler (6), Ivy (7), Jenner (8) and others which record the large incidence of carcinoma of the stomach in pernicious anemia.

Pathologically, the chronic atrophic gastritis in the chronic alcoholic is very similar to that of pernicious anemia. It is conceivable, therefore, that the functional deficiency is the same and the intestinal tract, including the colon, attempts to compensate for the deficiency in the production of the intrinsic factor. In the colon this results in foci of hyperplasia and adenoma formation.

Some support to this is seen in Ungley's (5) series of 9 cases of benign adenomas of the stomach in which 6 had pernicious anemia and 1 was alcoholic; and in the Kaplan and Rigler (6) report of 293 cases of pernicious anemia, 38 with carcinoma of the stomach, 7 with gastric polyps and 4 with carcinoma of the rectum and the colon.

Further evidence of the association of chronic alcoholism with adenoma and carcinoma of the rectum and the colon was found in a study of the autopsy records of the Los Angeles General Hospital from 1938 to 1947 inclusive in the following categories: polyps, carcinoma, subacute cirrhosis, Laennec's cirrhosis, fatty cirrhosis and fatty cirrhosis with an alcoholic history. There were 17 reports of adenoma (solitary type) of the rectum and the colon—one in a non-alcoholic, 7 in alcoholics, and in 9 not stated. Two of these 9 had Laennec's portal cirrhosis which is considered to be alcoholic in origin. The corrected figures then are: 1 or 6 per cent non-alcoholic; 9 or 53 percent alcoholic, and 7 or 41 per cent not stated. Assuming that these latter are non-alcoholic, the 53 per cent alcoholic remains a significant figure and corroborates the author's findings. The majority of the data concerning carcinoma was incomplete and no conclusions were possible.

This brings us to the second question, namely, from a practical point of view what clinical importance has this finding of high incidence of adenoma of the rectum in alcoholics. It is generally accepted that adenomas are definitely precancerous tumors and that 65 per cent or more eventually become malignant (Weber (9), Buie (10), Scarborough (11) etc.). (Figures 1, 2).

Carcinoma of the rectum and colon is the third most frequent malignant tumor in the body and it has been reported that each year in the United States 43,000 persons succumb to this disease. In addition, it is estimated (Bachus) (12) that there are 50,000 individuals who have this malignancy, totally unaware of its existence because of lack of subjective symptoms. In these, the diagnosis is delayed because symptoms often

TABLE III

NUMBER OF ADENOMAS IN EACH PATIENT
SIGMOIDOSCOPIC FINDINGS

	Non-Alcoholic				Alcoholic			
Number of	Female		Male		Female		Male	
Adenomas	No.	%	No.	%	No.	%	No.	%
1	68	75	92	76	20	100	85	72
2	14	16	22	19	0	0	19	16
3	2	2	3	2	0	0	9	8
Several	5	7	4	3	0	0	5	4
Total	89	100	121	100	20	100	118	100

TABLE IV

SIZE OF THE ADENOMAS
SIGMOIDOSCOPIC FINDINGS

	Non-Alcoholic				Alcoholic			
	Female		Male		Female		Male	
Size	No.	%	No.	%	No.	%	No.	%
1-4 mm.	26	29	35	29	6	30	27	23
5-9 mm.	44	50	54	45	11	55	64	54
10-19 mm.	17	19	28	23	3	15	25	21
20 mm.+	2	2	4	3	0	0	2	2
Total	89	100	121	100	20	100	118	100
Largest	25 mm.		25 mm.		10 mm.		30 mm.	

develop late, most individuals defer medical consultation and finally proctologic problems often are negligently handled.

Yet these thousands of adenomas and carcinomas, more than 70 per cent of which are located within the lower 10 inches of the colon (Jackman, Neibling and Waugh) (13), are waiting to be discovered and the majority of them can be identified early enough to prevent or cure a malignancy.

Ideally, this means routine sigmoidoscopy at regular intervals, even in the absence of symptoms. That, is not impossible. The inclusion of a sigmoidoscopic examination in every general physical examination would certainly be a major step in the early disclosure of many of these tumors. This certainly is indicated for the middle and older age groups.

According to the report on Alcoholism by a Special Committee of the California Medical Association (14) there are 750,000 chronic alcoholics and 2,250,000 borderline excessive drinkers in the United States. In view of the frequent incidence of adenomas in alcoholics, alcoholism becomes an important and practical means for selecting a large group of individuals who should routinely be sigmoidoscoped.

On June 8, 1949 Weber (9) presented a paper before the Section on Radiology at the 4th Annual Session of the American Medical Association in which in his plea for an earlier diagnosis of intestinal cancer, he hoped for some test or clinical syndrome which would indicate the existence of cancer before the disease has attained microscopic proportions. Whether or not alcoholism is a factor in carcinogenesis, the data presented indicate that this large group of individuals should have routine X-Ray examinations of the colon to discover, as early as possible, adenomas and carcinomas above the reach of the sigmoidoscope.

SUMMARY

The incidence of adenoma of the rectum and the sigmoid is much greater in alcoholics than in non-alcoholics. In a series of 5,980 patients sigmoidoscopy disclosed these tumors in 3.37 per cent of the non-alcoholic females and 5.46 per cent of the non-alcoholic males in contrast to 11.56 per cent of the alcoholic females and 18.23 per cent of the alcoholic males.

In view of the great malignant potential of this tumor these findings become significant. Alcoholism, therefore, identifies a group of 3,000,000 individuals for whom routine sigmoidoscopy is of great value for the prevention and possible cure of cancer.

A plea is made for routine sigmoidoscopy and X-Ray examination of the colon of all patients suffering from chronic alcoholism.

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CARCINOMA OF THE ESOPHAGUS

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THERE WERE 3000 deaths from carcinoma of the esophagus in the United States last year. About 2 per cent of all cancer deaths are due to carcinoma of the esophagus. In general carcinoma of the esophagus in about 80 per cent of the cases occurs in males and in 20 per cent in females. It occurs more frequently in the ages between 40 and 60.

Watson and Pool (21) feel that the carcinomas of the upper or cervical esophagus differ somewhat from carcinomas in the remaining portions of the esophagus in that they occur at an earlier age and are noted with relatively greater frequency in women.

In Sweden there is a higher incidence of carcinoma of the esophagus in females; about 40 per cent of the carcinomas occurring in females. In Sweden, women are prone to get an atrophy or a condition of the esophagus known as Plummer-Vinson syndrome which predisposes to carcinoma of the esophagus.

Carcinoma of the esophagus is especially prevalent in some countries. In China it makes up half the neoplasms of the alimentary tract. In China also carcinoma of the hypopharynx is much more frequent than in other countries.

Possibly oral infections, the rough character of certain foods, the irritating quality of some drinks may have to do with the etiology of carcinoma of the esophagus. Atrophic conditions of the esophagus play a part in its causation. In some countries syphilis is an etio-

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logical factor. Carcinoma of the esophagus occurs in cases of long standing strictures. Benedict (2) collected 33 such cases, 16 of which were due to the ingestion of lye.

Ochsner (14) in 8572 cases of carcinoma of the esophagus collected from the medical literature, found that 20 per cent developed in the upper third of the esophagus, 37 per cent in the middle third and 43 per cent in the lower third. The carcinomas are prone to occur at the areas in which the esophagus is narrow. The narrowest and most rigid portion is at the level of the cricoid cartilage. This narrowness extends for about a distance of 1 centimeter. The second area of narrowing is in the region of the arch of the aorta and the left main bronchus, where the narrowness extends about four to six centimeters in length. The third area of narrowing which measures one to two centimeters in length occurs at the diaphragmatic hiatus.

Grossly, carcinoma of the esophagus is an ulcerative tumefaction and in the majority of cases produces obstruction. Mathews (12) in a review of 237 autopsies of patients with carcinoma of the esophagus found that all except 22 had obstruction. The esophageal tumors are also associated with considerable formation of connective tissue.

*Histology*s Most carcinomas are squamous cell carcinomas. Borders (4) in 207 esophageal carcinomas found no grade I tumors, 16 or 8 per cent grade II, 95 or 45 per cent grade III and 93 or 46 per cent grade IV. Adenocarcinoma is sometimes found in the esophagus, but when this occurs it is probably due to the fact that the carcinoma arose from the cardiac end of the stomach and involved the esophagus secondly. It is also probable that many of the lesions found in the upper end of the esophagus are post-cricoid carcinomas or carcinomas of the hypopharynx, which have invaded the upper part of the esophagus secondarily.

These undifferentiated squamous cell carcinomas of the esophagus metastasize early. Since most of them are ulcerated, a great deal of infection may be present. The thin wall of the esophagus also makes it easier for these carcinomas to extend beyond their local site and also for the infection to spread beyond the esophageal wall.

Carcinoma of the upper third of the esophagus may involve the carotid arteries, the pleura, the recurrent laryngeal nerves and the trachea. Carcinoma of the middle third may invade the bronchus, thoracic duct, the aortic arch, the subclavian artery, the costal artery, the azygous vein and the right pleura. Carcinoma of the lower third may invade the pericardium, the left auricle, the left pleura and the descending aorta. Along with the tumor spread may occur inflammatory lesions of the mediastinum, of the pleura and of the lung. Necrotizing broncho-pneumonia and gangrene are very commonly found because of the frequent invasion of the trachea, the left main bronchus and the lung itself.

The lymph nodes involved in carcinoma of the upper third of the esophagus are those of the anterior jugular chain and the supraclavicular region. Carcinoma of the middle third may metastasize to the mediastinum and to the subdiaphragmatic lymph nodes occasionally. Carcinoma of the lower third predominantly metastasizes to the abdominal lymph nodes. Churchill (5) in 72 cases of carcinoma of the esophagus found only one out of 24 cases of the upper third, 11 out of 32 cases of the middle third, but 8 out of 16 cases of the lower third, which had metastasized to the subdiaphragmatic lymph nodes. Sweet (18) found 15 of 30 cases of carcinoma of the middle third of the esophagus to have metastasized to the abdominal lymph nodes.

Dormanns (7) gives table 1 showing the distribution of metastases according to the level of carcinoma of the esophagus.

Most diagnoses of carcinoma of the esophagus are made by x-ray examination in patients complaining of food "sticking" in the course of the esophagus. However, Brewer and Dolley (3) found a third of their cases of carcinoma of the esophagus by routine x-ray examination of the esophagus in cases referred for a roentgenological study of the stomach.

THE TREATMENT OF CARCINOMA OF THE ESOPHAGUS

Surgical Treatment: Torek in 1913 was the first one to successfully remove a carcinoma of the esophagus. The patient was alive 13 years after the operation and died of old age without any signs of recurrence. An artificial tube connected the esophagus to the stomach. Since that time Phemister, Adams, Garlock, Ochsner, Turner, Sweet and Churchill and others have successfully removed carcinomas of the esophagus. This in a great part has been due to better anesthesia (usually endotracheal cyclopropane-ether-oxygen), better control of intrapulmonary pressure (insufflation of the collapsed lung repeatedly during operation reduces post-

TABLE 1

DISTRIBUTION OF METASTASES ACCORDING TO LEVEL OF CARCINOMA OF THE ESOPHAGUS (DORMANNS)

Organs	Upper third (121 cases)	Middle third (418 cases)	Lower third (285 cases)	All (824 cases)
Lymph nodes				
Supraclavicular	6	20	12	38
Infraclavicular	1	5	1	7
Peritracheal and periesophageal	84	99	37	220
Mediastinal	28	231	147	406
Abdominal	11	104	121	236
Liver	20 (16%)	122 (29%)	122 (43%)	264 (32%)
Lungs and pleura	38 (31%)	82 (20%)	56 (20%)	176 (21%)
Bone	11 (9%)	31 (7%)	26 (9%)	68 (8%)
Kidney	5	30	24	59
Omentum and peritoneum	2	15	27	44
Suprarenal glands	4	10	21	35

operative atelectasis), more liberal use of blood transfusions for maintenance of the circulation and respiration, the routine use of penicillin and streptomycin and especially the better technique of esophagogastric anastomosis as the result of animal experiments and experience in the human operation.

Esophagogastrostomy, if possible, is done in every case even in carcinomas of the upper third of the esophagus. The connecting of the lower end of the esophagus and the upper end of the stomach by means of an external or a skin graft (Wookey operation) is only done when an internal esophagogastrostomy isn't feasible.

There are many contra-indications to surgery in carcinoma of the esophagus.

1. Bronchoscopic and esophagoscopic examination showing involvement of the bronchus and other structures.

2. Carcinomas located between the levels of the aortic arch and the left main bronchus rapidly invade, and become fixed to these structures and for this reason are practically never operable.

3. The finding of metastases to the rectal shelf is a contra-indication to surgery.

4. The presence of laryngeal paralysis is a contra-indication.

5. Bad general condition of the patient is a contra-indication to surgical excision.

6. Short, stout individuals have a high operative mortality.

7. The presence of pain usually means invasion of neighboring structures and probably inoperability.

8. If at the time of exploration of the tumor of the chest, there is almost complete or complete fixation, this is a contra-indication to surgical removal for quick recurrences occur.

9. Lesions high up in the upper third are also very difficult to remove and it is very hard to bring up the stomach high enough in order to do an anastomosis.

Fortunately most of the carcinomas, about 85 per cent of them, occur in the middle and the lower thirds of the esophagus, which can be more easily removed. However, these carcinomas metastasize to the abdominal lymph nodes and the abdomen must be explored before surgical removal is done. Metastases do occur quite frequently from carcinomas of the middle and lower thirds. Of 30 patients operated on by Sweet (18) with resection of the midportion of the esophagus, 15 already had abdominal metastases and esophagectomy was possible in only eight. Adams (1) in 100 consecutive cases of carcinoma of the esophagus reported that he could explore only 28 of these cases and in only 16 could a resection be done.

The postoperative mortality is still high. Strieder (17) reports the resection mortality for anastomosis below the arch, to be 12 per cent and 55.5 per cent for anastomosis above the arch. Sweet (18) in 22 consecutive excisions of the esophagus reports six operative deaths or about 30 per cent. The causes of death after surgery are usually empyema, pneumonia, peritonitis, fistulas, accidents common to older people, such as pulmonary embolism, heart failure, respiratory failure, cerebral accidents and coronary thrombosis.

RADIATION TREATMENT OF CARCINOMA OF THE ESOPHAGUS

Roentgen Treatments The technic of treatment of carcinoma of the esophagus by radiation therapy has greatly improved lately and the results have been very much better. This is due to two main reasons; first, to the multiple port technique and secondly, to the rotation type of therapy.

By means of a protractor the skin area about the carcinoma of the esophagus can be divided into 12 to 14 fields, each 10 x 10 centimeters. Each of these skin fields in rotation receives in divided doses 2000 roentgens measured in air or 2700 roentgens measured on the skin. The esophagus, about 14 centimeters away, thus receives about 6500 roentgens. This is a cancerolytic dose. Usually 100 to 175 r are given to each of two ports daily. The total treatment time is about five weeks. Instead of treating consecutive fields, the area treated may be alternated. In this way radiation pneumonitis is avoided. Radiation pneumonitis is also prevented by giving dicumarol by mouth.

Carcinoma of the esophagus is especially suitable for rotation x-ray therapy because the esophagus is situated in an almost central location in the longitudinal axis of the thorax. The patient is seated upon a turntable which turns about once per minute. Nielsen (13) found that the best results were obtained when a tumor dose of 5000 r was given over a period of 30 to 40 days. The daily tumor dose is 150 r given in two sittings. This type of rotation therapy produces a circular band of erythema and tanning about the chest. In four-fifths of Nielsen's patients who received more than 4000 r, complete or nearly complete immediate relief from symptoms was obtained. The patient could swallow without trouble. There was radiographic evidence of improvement. By this method a 25 per cent, twelve month survival cure was obtained against a former 10 per cent and a 15 per cent against a former 4 per cent two year cure.

When the multiple port technique and the rotation technique can be combined with x-ray therapy of a million volts or more results probably should be better.

Radium Treatment: Radium in the bougie forms and the interstitial implantation of radium through an esophagoscope have been practically abandoned, although occasionally one reports a success by the use of these types of treatment. The use of intracavitary radium seems to increase the duration of survival about two months.

Before radium can be used in the bougie form, a palliative gastrostomy is done. The patient is allowed to swallow a string which is removed through the gastrostomy. The string is attached to the radium applicator which is brought to the area of the carcinoma under fluoroscopic control. The esophageal instrument contains about 30 milligrams of radium filtered with .5 millimeter of platinum. It is left in place for 24 hours after which it is removed and replaced again 24 hours later. The process is repeated until 2800 or 3000 milligram-hours are given as a total dose. Usually this treatment is supplemented by external roentgen ray therapy through six or as many ports of 10 x 10 cm. as possible, directed towards the carcinoma of the esophagus. The factors usually used are

200 kvp. or more, .5 millimeter of copper and 1 millimeter of aluminum filtration, and 50 to 100 cm. skin focal distance.

The successful treatment of carcinoma of the esophagus by radium in many cases resulted in a perforation of the esophagus with mediastinitis and death.

THE RESULTS OF TREATMENT OF CARCINOMA OF THE ESOPHAGUS

The average life of untreated patients with carcinoma of the esophagus is very short. Greenwood (10) in 299 untreated patients reported that 25 per cent were dead within six months, 50 per cent were dead within eight months and 75 per cent within one year. Adams (1) reports the average time between the first symptom and death, ranges between five and eight months. The duration is not influenced apparently by the age of the patient or the location or type of the tumor.

The results of recent methods of surgical treatment are very good when compared to the old methods. Vinson (19) in 1000 cases of carcinoma of the esophagus could operate on only 24 or 2.4 per cent. The mortality was high, ranging from 48.5 per cent as found by Von Winiwarter (20) to 70 per cent as found by Eggers (8). In the past, only 5 or 6 per cent of the patients resected lived five years. Recently with all the improvements, surgery is more successful. Adams (1) in 1944 reported a series of 16 resected lesions with three patients living two years or more or 19 per cent. Garlock (9) in 1944, of 16 resected lesions reported 7 or 44 per cent living up to two years and 4 for more than three years.

The results of treatment with radiation previous to the present decade also were extremely discouraging. Cleminson (6) treated 89 cases and found the average survival period after treatment to be five or six months, about two months longer than untreated patients. The use of radium bougies and gold radon seeds seems to increase the life expectancy also about two months.

Recently with higher kilovoltage, multiple port technique and rotation technique, the results have been more successful. Pohle and Benson (15) reported two carcinomas of the upper end of the esophagus treated by roentgen irradiation alone in one case, and with roentgen irradiation and the implantation of radon seeds in another. The first patient is well for four years and the second case is alive and well for over seven years. Both cases were confirmed histopathologically.

Jacobsen (1) in a poorly differentiated squamous cell carcinoma about five centimeters long just above the diaphragm, obtained a six year cure with a tumor dose of over 5000 roentgens given over a period of 35 days.

Smithers (16) treated 80 patients and 20 lived one year or longer. Three of them or 4 per cent lived five years. Of 32 patients treated over two years ago, 4 or 12 per cent are still alive.

Nielsen with rotation therapy obtains 25 per cent one year survival rate contrasted with 10 per cent by older methods and 15 per cent two year survival rate contrasted to a previous 4 per cent.

For tabulated results of treatment of carcinoma of the esophagus see table 2.

TABLE 2

COMPILED RESULTS OF TREATMENT OF CARCINOMA OF THE ESOPHAGUS WITH OPERATION ONLY, OPERATION WITH IRRADIATION AND IRRADIATION ONLY

Operation Only				Operation with Irradiation				Irradiation Only			
		Living 5 Years				Living 5 years				Living 5 years	
Author	Total No. of Cases	No. of Cases	%	Author	Total No. of Cases	No. of Cases	%	Author	Tot.l No. of Cases	No. of Cases	%
Previous to 1938											
Vinson	24	0	0.0					Vinson	50	0	0.0
								Finzi		2	
Von Winiwarter	35	1	3.85 (18 mos.)					Cleminson (7)	89	0	0.0
								Colledge (8)		1	(2 yrs.)
C. Eggers	17	1	5.8 (18 mos.)					Howarth (9)		1	(3 yrs.)
Perla	17							Guisez (10)	207	11	4. (3 yrs.)
Torek		1						Mailer (11)	11	5	45. (1 yr.)
Since 1938											
Phemister (1942) (1)	4	1	25. (1 yr.)								
								Smithers (Rev. literature to 1944)		10	(5 yrs.)
Adams (1944) (2)	16	3	19. (1-2 yrs.)					Smithers (12)	32	4	12. (2 yrs.)
								Smithers		3	(5 yrs.)
Garlock (1944) (3)	16	7	44. (1-2 yrs.)								
Garlock		4	25. (3+ yrs.)					Jacobson (13)		1	(6 yrs.)
De Freitas, et al	14	4	28. (1+ yrs.)								
								Nielsen (14)	17	2	15. (2 yrs.)
Sweet (1947) (4)	31	12	38.7 (3 yrs.)								
								Pohle and Benson (15)		2	(4-5 yrs.)
Strieder (5)	26	21	80. (1-40 mos.)								
Watson & Pool (1948) (6)		1	(7 yrs.)	Watson and Pool		2 (10 yrs.)					

FOOTNOTES TO TABLE 2

(1) *Phemister*: Of six patients, four survived the operation. Of the four cases of esophageal resection through the thorax and neck, one patient died eight days after the operation, one is alive after 7 months and two died of recurrences 10 and 14 months respectively, after operation.

(2) *Adams*: resected 16 cases, 3 are alive 12, 16 and 25 months after operation.

(3) *Garlock*: Of 16 patients resected, 8 died of recurrence from 9 months to 2 years following operation, one died of coronary thrombosis and 7 remained without evidence of disease, 4 of these for more than 3 years.

(4) *Sweet*: In the early postoperative period, the most frequent single cause of death was congestive failure of the heart, which accounted for 9 of the 23 fatalities. The next most frequent cause of death was sepsis, which occurred in 5 cases. Of 91 patients operated on for carcinoma of the lower part of the esophagus and cardia, there were 30 whose operation was performed 3 or more years ago. Seven of these patients died as a result of operation (25%), leaving 23 who had an opportunity to survive. Nine of these 23 patients were alive 3 or more years after operation. This represents a 3 years survival rate of 39 per cent. Of the 50 patients in whom resection of carcinoma of the mid-thoracic esophagus was performed since 1944, there were 11 hospital deaths. Of the 39 surviving, 8 had their operations in 1944 and 3 of these (37%) are alive and apparently well over 2 years after operation.

In 1948, Sweet reports the immediate results of resection of carcinoma of the esophagus and cardia as follows:

IMMEDIATE RESULTS IN CARCINOMA OF THE ESOPHAGUS AND CARDIA (PRIMARY ANASTOMOSIS GROUP) —SWEET

Location	No. Cases	Complications with Recovery	Deaths	Mortality Per Cent
Cervical esophagus, Wookey technique	7	2	0	0
Superior mediastinal segment	1	0	0	0
Midthoracic segment	72	12	17	23.6
Lower thoracic and abdominal segments	23	7	3	13
Gastric carcinoma invading the cardia and lower esophagus	86	16	10	11.6
Total	189	37	30	15.9

(5) *Strieder*: Prior to 1945 there were 35 cases in which an anastomosis could be done below the arch of the aorta. The operative mortality was 24 per cent. There were 12 cases in which the anastomosis had to be done above the aorta. The operative mortality was 63.6 per cent. For the period 1945-1947, the operative mortality was 12 per cent for the anastomosis below the arch and 55.5 per cent above the arch Of 26 operative survivors, 21 are still alive from 1 to 14 months later.

(6) *Watson and Pool*: Two patients with advanced carcinoma of the cervical esophagus, treated by a combination of radiation and surgery, were alive and well ten and ten and one-half years, respectively. One patient had a surgical extirpation of the carcinoma of the cervical esophagus and a surgical, skin-lined, tubular reconstruction 7 years previously, and is alive and free of disease at the time of this communication.

(7) *Clemson* treated 89 cases and found the average survival period after treatment to be five or six months.

(8) *Colledge*, by using seeds in a carcinoma of the lower third of the esophagus, kept one patient alive for 2 years.

(9) *Howarth* had a patient live 3 years by applying ten, one millicurie radon seeds to a carcinoma in the upper third of the esophagus.

(10) *Guisez*, in a series of 270 cases treated with radium bougie, found 11 patients or 4 per cent surviving 3 years.

(11) *Mailer* treated 11 cases of carcinoma of the lower third of the esophagus. A gastrostomy was first performed, and by means of a string swallowed and then drawn out through the gastrostomy opening, 30 milligrams of radium, in five milligram needles arranged in tandem, were applied to the tumor under fluoroscopic control. By this treatment, stenosis of the esophagus usually occurred, which was gradually dilated by bougies. After the dilatation the gastrostomy opening was allowed to heal.

(12) *Smithers*: Of 32 patients adequately treated, Smithers found 30 with marked alleviation of symptoms and 14 lived more than 1 year, 5 beyond 2 years and 3 for 5 years.

(13) *Jacobsson's* case was a poorly differentiated squamous cell carcinoma 5 centimeters long just above the esophagus. The tumor dose was 5000 r in 35 days.

(14) *Nielsen*: In 17 patients in whom an adequate tumor dose could be delivered, 8 lived one year, 2 were alive and symptom free at the end of two and a half years and three and a half years, respectively.

In 140 patients an attempt at curative x-ray therapy was made, using the rotation method; 96 of these patients received more than 4000 r into the substance of the esophageal carcinomas. In four-fifths of Nielsen's patients, who received the full dose, complete or nearly complete immediate freedom from symptoms was obtained. The patients could swallow and there was radiographic evidence of improvement. Death was due to metastases and cachexia, but the majority of patients were able to swallow until the fatal day. The survival cure for months and years revealed that with rotation x-ray therapy, 25 per cent of the patients as against a former 10 per cent were alive at the end of one year and 15 per cent as against a former 4 per cent, were alive at the end of two years.

(15) *Pohle and Benson's* cases were at the upper end of the esophagus. One treated by external roentgen ray alone is alive and well four years. Another case treated with irradiation and implantation of radon seeds is alive and well for over 7 years. Both cases were confirmed by microscopic examination.

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THE SURVIVAL OF THE LANSING STRAIN OF THE POLIOMYELITIS VIRUS IN ICE CREAM

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THE EPIDEMIOLOGY of poliomyelitis is still subject to investigation. The enteric route, however, has been implicated in a number of studies, some of them (1, 2) indicating transmission of this infection by milk and ice cream.

While the virus of poliomyelitis is inactivated by heating at 50° C for 3 minutes (3), it has been found to survive freezing at -70°C and -20°C for 12 months without loss of its titer (4). Lawson and Melnick (5) found that murine strains of the poliomyelitis virus suspended in milk withstood higher temperatures than the same viruses suspended in water. Thus it seemed of interest to study the survival of the Lansing strain of poliomyelitis virus in ice cream at different temperatures.

MATERIALS AND METHODS

The Lansing strain of poliomyelitis virus used in these experiments had a titer of 10^{-4}. A 10 percent suspension of it was prepared by grinding infected mouse brains with melted, hand packed ice cream in a sterile mortar. This ice cream mouse brain suspension was then placed in test tubes, in one ml. amounts. Saline suspensions of the virus were prepared in the same manner, using saline instead of ice cream as the vehicle. All suspensions were centrifuged at 2,000 r.p.m. for 15 minutes. The supernatants were then removed and considered as 10 percent dilutions of the virus.

EXPERIMENTAL PART

In the first series of experiments, tubes containing the ice cream-virus suspension and tubes with the saline-virus suspension were placed in a water bath at 55°C for 30 minutes. After heating, the suspensions were inoculated into groups of 24 mice each. This procedure was repeated, heating both the ice cream and saline-virus suspensions at 60°C, 65°C and 70°C for 30 minutes and inoculating groups of 24 mice with each heated suspension.

In the second series of experiments, ice cream and saline-virus suspension were placed in the refrigerator at 4°C and portions of them inoculated, at one month intervals, into groups of 12 mice. At the same time ice cream and saline suspensions were placed at room temperature at 20° to 21.5°C, and portions of them inoculated, at one month intervals, into groups of 12 mice. The mice were observed for clinical and pathological signs of poliomyelitis and the data recorded.

RESULTS

Table I shows the outcome of the first series of experiments in which the viability of the Lansing virus in ice cream was compared to that in saline suspension after heating at 55°, 60°, 65°, 70° and 75°C for 30 minutes. Ice cream seems to afford a certain pro-

TABLE I

SURVIVAL OF LANSING TYPE POLIOMYELITIS VIRUS AT 55° TO 75°C.

Virus suspended in	Suspension heated for 30' at C	No. mice died of polio/No. mice inoculated with virus suspension			
		10^{-1}	10^{-2}	10^{-3}	10^{-4}
Ice cream		17/24	11/24	11/24	5/24
Saline	55°	9/24	7/24	3/24	0/24
Ice cream		11/24	7/24	6/24	3/24
Saline	60°	0/24	0/24	0/24	0/24
Ice cream		5/24	2/24	0/24	0/24
Saline	65°	0/24	0/24	0/24	0/24
Ice cream		2/24	0/24	0/24	0/24
Saline	70°	0/24	0/24	0/24	0/24
Ice cream		0/24	0/24	0/24	0/24
Saline	75°	0/24	0/24	0/24	0/24
Ice cream		12/12	10/12	8/12	5/12
Saline	unheated	12/12	11/12	6/12	4/12

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TABLE II

SURVIVAL OF LANSING TYPE POLIOMYELITIS VIRUS AT 4°C AND 20° TO 21°C

Month of experiment.	Virus suspended in	Suspension kept at C°	No. mice died of polio/No. mice inoculated with virus suspension.			
			10^{-1}	10^{-2}	10^{-3}	10^{-4}
1	Ice cream	4	10/12	7/12	4/12	1/12
	Saline		5/12	3/12	1/12	1/12
	Ice cream	20-21	7/12	5/12	3/12	2/12
	Saline		5/12	4/12	1/12	1/12
2	Ice cream	4	7/12	5/12	3/12	0/12
	Saline		5/12	3/12	1/12	0/12
	Ice cream	20-21	5/12	4/12	2/12	2/12
	Saline		4/12	2/12	1/12	1/12
3	Ice cream	4	5/12	3/12	1/12	1/12
	Saline		2/12	1/12	0/12	1/12
	Ice cream	20-21	5/12	5/12	3/12	2/12
	Saline		2/12	1/12	0/12	0/12
4	Ice cream	4	3/12	1/12	1/12	0/12
	Saline		1/12	0/12	0/12	0/12
	Ice cream	20-21	3/12	2/12	1/12	0/12
	Saline		0/12	0/12	0/12	0/12
5	Ice cream	4	3/12	1/12	1/12	0/12
	Saline		0/12	0/12	0/12	0/12
	Ice cream	20-21	1/12	1/12	0/12	0/12
	Saline		0/12	0/12	0/12	0/12
6	Ice cream	4	1/12	0/12	0/12	0/12
	Saline		0/12	0/12	0/12	0/12
	Ice cream	20-21	0/12	0/12	0/12	0/12
	Saline		0/12	0/12	0/12	0/12

tection to the virus against higher temperatures, the virus surviving at temperatures as much as 10°C higher in ice cream than in saline.

Table II demonstrates the survival time of the Lansing strain at 4°C and at room temperature. The virus, while attenuated, survived in ice cream for 5 months in the refrigerator. Its presence could be proven, at least for 4 months, also at room temperature, by mouse experiments in that medium.

DISCUSSION AND SUMMARY

The Lansing poliomyelitis virus suspended in ice cream was more resistant to heat than in saline suspension. Virus suspended in ice cream and kept in the refrigerator survived for 5 months, at room temperature for 4 months. This period was longer than the survival time of the same virus in saline. The number of variables which affect this type of experiment are, however, great. Thus a definite judgment about the thermostability of the Lansing poliomyelitis virus cannot be made readily. The most probable explanation for the prolonged survival of the Lansing virus in ice cream, however, is the physical protective action of this food.

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ABSTRACTS ON NUTRITION

CHELDELIN, V. H.: *Nomenclature of the vitamins.* Nutrition Reviews, 9, 10, Oct. 1951, 289-292.

The author attempts to create order out of the relative chaos at present existing in vitamin nomenclature. Vitamins are now generally regarded as dietary essentials for higher animals only. A nutrilite is a "vitamin" for *any* organism. Vitamin K gets its name from the first letter in the German word Koagulation and is the first vitamin whose origin is not purely alphabetical. Others in this class are H = Haub (skin), L for lactation, M, a vitamin for monkeys, and P which prevents excessive cell permeability.

What was originally called vitamin B is now known as "B Complex" and the numbers B_1 to B_{14} refer to substances bearing little resemblance to one another in their physiological action.

B_2 (riboflavine) was known for several years as vitamin G, and pantothenic acid also bore this designation briefly. B_3, necessary for pigeons, is probably identical with pantothenic acid. B_4 has been alternately described as a mixture of arginine and glycine, or of riboflavine and B_6. B_5, a factor for pigeons, is probably the same as nicotinic acid. B_7, or vitamin I, extract of rice polishings useful to pigeons and probably a mixture of other nutrilites. B_8, adenylic acid, is not usually regarded as a vitamin as it enters into nucleic acids, as well as participating in phosphate transfer systems. B_9 is unused. B_{10} and B_{11} are reported to be chick-feathering and chick-growth factors, but are probably mixtures of folic acids and B_{12}. B_{12}, the "animal protein factor" or the antipernicious anemia factor, has related compounds—B_{12a}, B_{12b} B_{12c} and B_{12d}. B_{12a} and B_{12b} are thought to be identical. B_{13} is an uncharacterized vitamin discovered in distiller's dried solubles and promotes growth in rats. B_{14} was announced as a metabolite of xanthopterin (related to folic acid) but this announcement was probably premature. B_t is a growth factor for insects. Niacin is nicotinic acid or the P.P. factor. Biotin is vitamin H or Bios II or coenzyme R. Inositol is inosite or Bios I.

D_2 is irradiated ergosterol. D_3 is irradiated 7-dehydrocholesterol. The E vitamins include alpha-, beta- and gamma-tocopherol, all occurring naturally. Over 50 synthetic products possess E activity. Vitamin J, also called C_2, has been postulated as an antipneumonia principle. T is a group of factors from termites, yeasts and molds which produce gigantism in insects, in fact, every letter of the alphabet has been used to designate nutrilites. The citrovorum factor, a relative of folic acid, and protogen (B_{13}) are in line for intensive studies. The future of vitamins is unlimited. In the future alphabetical designations will not be used.

HOLTEN, C. AND LUNDBAEK, K.: *Metabolic and renal diabetes following the administration of ACTH*, Scandinavian J. Clin. Labor. Investig. 2, 4, 317. 1951.

Determinations of blood sugar and urine sugar under standardized ingestion of food in two patients suffering from spondylarthritis ankylopoetica showed that during the administration of ACTH in doses varying from 60 to 100 mg. daily there appeared a delayed fall of the blood sugar after administration of carbohydrates, and a glucosuria without any rise of fasting or maximum blood sugar values. It seems as if ACTH causes both a metabolic and a renal diabetes. Examinations of the content of glutathione in the blood under the influence of ACTH gave no unequivocal results.

Franz J. Lust.

NYE, L. J. J. AND FORREST, V.: *Treatment of vascular hypertension by low sodium diet.* Med. J. Australia, Aug. 4, 1951, 152-154.

The authors believe benefit in hypertension is to be obtained from the prolonged use of a low sodium diet; however they think Kempner's diet is too low in protein and they advocate 80 to 100 gm. protein daily. They found Australian aborigines, who never had any contact with salt, living to old age without hypertension or arteriosclerosis. They advise not more than 200 mg. of sodium daily and have had no instances of circulatory collapse. They provide handy dietary tables but do not divulge any of their results on blood pressure.

RATH, M. M.: *Hypochromic anemia in the aged.* Medical Times, 79, 10, Oct. 1951, 617-621.

Forty-seven subjects, 65 to 90 years of age, living in an institution for the aged, served in a study to determine the effect of iron alone as compared with iron combined with liver, vitamin B complex and ascorbic acid in the treatment of hypochromic anemia. The increase in red cells and hemoglobin was faster and greater in the groups receiving combined therapy than in those taking iron alone. In 6 weeks there was an average rise in red cells of 26.2 percent on combined therapy while iron alone required 38 weeks to produce

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an equal improvement. Hemoglobin rose as much in 9 weeks on combined therapy as in 32 weeks on iron alone. It is felt that in hypochromic anemia best results are obtained by adding B-complex, liver and ascorbic acid to the iron.

WEINSTEIN, J. J. AND LANE, G. F.: *Rapid infusions of invert sugar.* Med. Ann. District Columbia, XX, 4, April 1951, 186-192.

Invert sugar is a hydrolyzed product of sucrose consisting of equal moles of glucose and fructose. The results reported in this article with the rapid infusion (34 minutes) of a single infusion of 50 grams of invert sugar indicate 99.2 percent assimilation of that injected. By replacing glucose with invert sugar we can save time and inconvenience to the patient. Invert sugar appears to be a good substitute for glucose. It readily supplies calories and glycogen. It may not be long before simple positive caloric and nutritional balance in patients on total parenteral feeding may be accomplished. Fructose is a better glycogen-former than glucose even in the absence of insulin. Intravenous invert sugar is more readily utilized than is glucose in equal amounts. Twice as much invert sugar than dextrose, expressed as gms. per kilo of body weight, may be given intravenously with almost 100 percent utilization.

JOLLIFFE, N. AND ALPERT, E.: *The "performance index" as a method of estimating effectiveness of reducing regimens.* Postgraduate Med., 9, 2, Feb. 1951, 106-115.

Using the Boothby and Berkson Food Monogram (copies of which may be obtained from the Mayo Clinic), it is easy to figure the food allowance required for the ideal weight of the obese person, making due allowances for physical activity. By placing the patient on a diet conforming to this calculated food allowance, it is possible to predict the rate of weight loss, provided the patient follows the diet. The ratio of the ideal weight loss to the actual weight loss over a period of time represents the "performance index." The latter is valuable as an indicator of the patient's adherence to the prescribed diet. The authors also found that drinking 4 ounces of orange or grapefruit juice about an hour before meals is an effective anorexic agent.

PRIDDLE, W. W.: *Hypercholesteremia: an analysis of 529 cases and treatment of 297 by a low animal fat diet and desiccated thyroid substance,* Ann. Int. Med., 35, 4, Oct. 1951, 836-847.

In a series of 1089 patients studied, the serum cholesterol was over 250 mg. percent in 529, or 48.6 percent of cases. The level was over 300 mg. percent in 50.5 percent of the group with elevated serum cholesterol. The incidence of hypercholesteremia was 59 percent in patients over 40 years of age. Serum cholesterol levels were elevated in 72.5 percent of patients with arteriosclerosis. Coronary arteriosclerosis showed 69.7 percent with hypercholesteremia, and approximately the same percentage was established for retinal arteriosclerosis, hypertension and diabetes mellitus. The use of diets low in animal fat along with 1 to 3 gr. of thyroid substance daily produced an average lowering of cholesterol levels. The results were not marked or consistent. A low animal fat diet produced a lowering of serum cholesterol in 55 percent of individual cases. With the use of thyroid, and the combination of thyroid with low animal fat diet, the serum cholesterol was decreased in 45 percent of patients in each group. There may be many reasons for failure to obtain favorable results. Stark's rice diet with only 5 gm. of fat, used in 125 patients with hypertensive vascular disease, produced a substantial reduction in hypercholesteremia in 98.4 percent of cases. Finally, Gofman's work, tending to incriminate a particular class of lipid and lipoprotein molecules in the production of arteriosclerosis gives the subject a new orientation. Priddle intends to continue with his cases, reducing vegetable as well as animal fats.

KENNEDY, G. C.: *Experimental hypothalamic obesity.* Proc. Roy. Soc. Med., 44, 10, Oct. 1951, 899-902.

It was not until 1939 that Ranson was able to produce pure hypothalamic obesity experimentally, by making small electrolytic lesions in the brain with an electrode introduced from above, leaving the pituitary gland intact. In 1943 Brobeck et al improved the technique, used smaller lesions, got much more striking obesity and showed that bilateral damage to the nuclei of the tuber cinereum was the essential lesion. The original work was done on the rat but later confirmed in the cat, the dog and the monkey. The *immediate* cause of the obesity is overeating, and post-operatively for 6 weeks, the rats will consume two or three times as much food as a normal rat. Later, food intake decreases, often to normal, but obesity is maintained. If the animal is dieted to lose weight, he gains it all back, once normal diet is restored. Such operated rats seldom survive more than one-half their normal life span. The kidneys and adrenals enlarge and there is marked albuminuria. The animals become "fussy" about their food (whereas normal rats are not) and will not eat food mixed with dry Kaolin powder. Restriction of water causes decreased food intake. Hunger itself probably has nothing to do with the hypothalamus. Hunger stops as soon as hyperphagia has produced marked obesity. Normally the hypothalamus probably exerts an inhibiting effect on appetite, due to its response to circulating metabolites. As in older, operated rats, so with most obese humans, the hypothalamus is of less importance than the lack of cortical control.

EDITORIALS

PROLAPSE OF GASTRIC MUCOSA INTO THE DUODENAL BULB

Recently, Levin and Felson (1) carried out upper gastrointestinal x-ray studies on 100 patients who had no gastrointestinal symptoms of any kind. Prolapse of the gastric mucosa into the duodenum was encountered in 18 cases. They *logically* conclude that the condition is not one of great clinical importance, and seldom causes symptoms. However, the matter is not quite so easily settled. For example, the literature contains many cases in whom digestive symptoms disappeared after the surgical correction of the condition. If we are not mistaken, one might find gall bladder disease in 18 percent of persons having no digestive symptoms, were he to look for it carefully. The contribution of Levin and Felson is valuable but it does not spell "finis" to one of our newer diseases. Incidentally, the x-ray diagnosis of prolapsed mucosa is difficult and Levin and Felson's criteria should be adhered to. We feel that the examination of persons *with* digestive symptoms might have proved more reliable.

(1) Levin, E. J. and Felson, B.: Asymptomatic gastric mucosal prolapse. Radiology, 57, 4, Oct. 1951, 514-520.

THE FOLLY OF TOO MUCH DOGMATISM IN HUMAN DIET

The recent report by Johnson and Rynearson from the Mayo Clinic, of a diabetic patient who subsisted on an extremely high-fat, low-carbohydrate and low protein diet for 28 years without developing the degenerative features of diabetes, is one which, added to many others, increases the realization of our essential ignorance of the basic causes of arteriosclerosis. Furthermore, our ignorance on this subject is not more profound than our lack of ultimate knowledge with respect to the relationship between health and diet in general.

The writer was consulted by a beautiful woman who

looked 35 but was actually 60 and in excellent health, although she professed, with some sense of guilt, that for forty years she had subsisted almost *exclusively* on bread and butter and tea, merely because she liked this diet and it agreed with her. The writer, after examining her, saw no reason to change her eating habits or to add vitamin supplements.

Of course, we cannot explain *why* this patient at Mayo Clinic remained an extremely healthy diabetic in spite of a very high fat diet or why the woman mentioned failed to develop vitamin deficiency diseases or anemia. The explanation would require further intensive study of both cases, However, the time element may be of importance. The body, unable to do certain things in a short time, may indeed be capable of doing them over a long period of time. Thus, have we any information as to whether a diet which, in short periods would result in vitamin deficiency disease or liver disease, might not if gradually adopted and adhered to over long terms, fail to produce such changes? There is always the possibility that certain nutrients considered essential might, contrary to current opinion, either be manufactured by an organism under prolonged stress through their absence, or efficiently substituted for by some deviation of metabolism which at the moment escapes our attention.

The *practical lesson* from such considerations is to the effect that no matter how wrong a patient's diet may seem from an academic or clinical point of view, it *must* be a good diet if, over a period of years, it has maintained health and failed to give rise to what we call nutritional disease.

BOOK REVIEWS

STUDIES ON THE CEPHALIC PHASE OF GASTRIC SECRETION IN MAN, PARTICULARLY FOLLOWING PARTIAL GASTRECTOMY. Ove Noring. (Copenhagen). Borens Forlag, Kobenhavn, 1951. 235 pages 54 tables.

The main object of the book is the significance of the pyloric part in the mechanism of sham feeding secretion. For this purpose the writer studied the sham feeding secretion before and after partial gastrectomy. Tests conducted 11-14 days after this operation showed a marked reduction in the volume of sham feeding secretion as well as its acidity and total chloride, whereas the secretion of pepsin was not found to be significantly reduced. This reduction in the cephalic phase might be imagined to be a temporary phenomenon. The same test was therefore made 2-36 months after the operation. This showed a further reduction in all the components of gastric secretion. In analogy with the sham feeding test, Noring submitted other ulcer patients to insulin tests to produce gastric secretion due to hypoglycemia which secretion is of cephalic origin. These experiments showed a marked reduction in the cephalic secretion 11-14 days after partial gastrectomy and a further reduction 3-36 months after the operation.

Another chapter deals with the fasting morning secretion the origin of which is discussed. Despite the heterogeneous nature, certain circumstances indicate that its formation is due, in part at least, to nervous causes. There are marked individual variations in its volume, acidity, total chlorides, and pepsin values, variations which are more marked among ulcer patients than among normal subjects, just as in the sham feeding secretion. Moreover, the morning secretion is on the average larger and more acid in ulcer patients than in normals. Attaching most importance to the sham feeding studies, it seems reasonable to draw the conclusion that the resected part of the stomach has been a link in the processes which elicit the cephalic phase of gastric secretion.

The book has a good bibliography of 240 numbers, it is well printed. The text is in Danish with a long summary in English. It is of the greatest interest to all those interested in gastroenterology and physiology.

Franz J. Lust.

YOUR DIABETES. A manual for the patient. Herbert Pollack, M. D. and Mary V. Krause, M. S., Paul B. Hoeber, Inc., New York, 1951, $3.00.

Pollack adds an unusually good book to the rather large number of books which have been written in recent years by physicians for patients. Possibly this tendency to write helpfully in lay language has been most pronounced in diabetes, perhaps because of the necessity for technical knowledge on the part of the patient himself. The present volume strikes the reviewer as being as good as any that has been written and better than many of them. There is an important element of cheer and inspiration running through the volume, so pronounced as possibly to make the diabetic rather glad that he acquired the disease. Hardening of the arteries is mentioned but not emphasized and in our present state of ignorance of this subject, Pollack's attitude is to be admired. Nothing of importance has been omitted and the book may well be recommended to the patient.

THE SCOTTISH CHEMIST'S INDEX OF MODERN REMEDIES. Published by the Scottish Chemist. Glasgow S1, Scotland, 1951, $2.00 (Order from The Scottish Chemist, Box 275, Terminal A, Toronto, Canada).

This volume represents an excellent attempt to clarify the names and significances of the many and various modern remedies used in Great Britain, Canada and the U. S. A. A representative list of pharmaceutical houses is included as well as a useful index. It would be particularly useful to those U. S. physicians who read British medical journals and vice versa and to Canadians who read both. The Canadian addresses of both British and U. S. pharmaceutical firms are supplied.

FIRST ANNUAL REPORT OF STRESS, Hans Seyle, Acta, Inc., Montreal, 1951.

To use a slang expression, this is *some* book. Every physician today has become to some extent familiar with the ideas of Seyle which, taken as a whole, tend to interpret life as a resultant of the organism's vitality versus the "stress" to which it is subjected. Thus far, and as just stated, this is not a new philosophy, since most biologists for the past 60 or 70 years have regarded life as a reaction of the organism to its environment. (Of course the *further* philosophical question arises as to whether life is anything *else* beyond a reaction to stress or strain). What is comparatively new is a mass of scientific facts which superficially at least indicate that some diseases are specifically stress reactions, involving the glands of internal secretion and producing organic changes in various bodily organs. Such facts may legitimately be interpreted as complex hormonal reactions to stress, in which it has been possible to follow, with some certainty, the chain of events which being initiated by stress, ultimately culminate in serious and irreversible organic or physiological lesions. This volume is the first of a series of annual volumes which attempt to tabulate, if not correlate, various scientific findings bearing on the main theory.

Seyle's own personality, as he admits, breathes through the book. Today the great stress theory is, in a sense, a creation of this unusual man, to whom we readily pay the tribute of tremendous industry and brave thinking. Whether Seyle or anyone will eventually be able to constitute stress as possibly the main factor in all disease is an open question. In the interim, the work deserves careful study, even though it behooves everyone to maintain the usual skeptical balance, even when the author gives some present promise of becoming one of medicine's great men!

AMER. JOUR. DIG. DIS.

GENERAL ABSTRACTS OF CURRENT LITERATURE

FELDMAN, M.: *Prolapse of the gastric mucosa into the duodenal bulb: a problem for investigative study.* Rev. Brasil. Gastroent., 3, 4, July-August, 1951, 395-402.

Prolapse of the gastric mucosa into the duodenum has not been observed in any of the author's patients who were previously subjected to vagal resection. Anticholinergic or nerve-blocking agents may be useful as a physiological test and as a means of relief of symptoms. Prolapse of gastric mucosa at present is a controversial subject. Not all radiologists and gastroenterologists are prepared to make such a diagnosis.

DORIA, O. DE B. S.: *Total gastrectomy.* Rev. Brasil. Gastroent., 3, 4, July-August, 1951, 403-14.

This is a description of total gastrectomy and a report of 2 cases of the operation done by the trans-thoraco-diaphragmatic approach, one a case of carcinoma, the other proving histologically to be a case of hypertrophic gastritis, erroneously diagnosed as cancer pre-operatively.

WILSON, I. S.: *A review of chronic amebiasis in returned service personnel.* New Zealand M. J., XLIX, 273, Oct. 1950.

In a series of 148 returned soldiers who were discovered to be suffering from amebiasis after arrival in New Zealand, 85 percent had never been diagnosed overseas. In 10 percent the entameba was not found, but the diagnosis was established by the response to treatment. In only one case where the parasite was not found did sigmoidoscopy suggest the diagnosis. Prior to the discovery of amebiasis, 14 percent had been diagnosed as dyspepsia and 14 percent as anxiety neurosis. After treatment, 31.5 percent were apparently cured and 60 percent were improved. There was no improvement in 8.5 percent, and these were found to be suffering from some other disability with the amebic infection in an inactive or carrier state.

SHAEFFER, J. R. AND PULASKI, E. J. *Antibiotics in gastro-intestinal surgery.* U. S. Armed Forces M. J., 1, 12, Dec. 1950.

For sterilizing the human gut the authors have 2 preferences, (a) the nonabsorbable sulfonamides, (b) streptomycin with glucurono-lactone. For controlling secondary peritonitis they have found terramycin to be the most singly effective agent, 1 gram intravenously every 12 hours.

TERRY, K.: *Erythrocyte sedimentation in anemia.* Brit. Med. J., Dec. 9, 1950.

The author presents theoretical, clinical and experimental reasons for believing that the erythrocyte sedimentation rate is not increased by anemia, and hence the observed readings have the same significance in anemia as in normal blood states. In fact it would appear that the suspension stability of red cells is increased in anemia.

ANDERSON, J. R., DOCKERTY, M. B. AND WAUGH, J. M.: *Peritoneoscopy: an evaluation of 369 examinations.* (Proc. Staff Meet. Mayo Clin., 25, 22, 1950, 601-605).

When peritoneoscopy was performed to confirm a clinical diagnosis, the correct diagnosis as established by follow-up was made by peritoneoscopy in 93.3 percent of cases. When peritoneoscopy was performed to establish a diagnosis from an array of possibilities, the correct diagnosis was established by this method in 71.1 percent of cases. It was of limited value in determining the resectability of malignant tumors. In only one instance out of 392 cases could death be attributed to accident resulting from peritoneoscopy.

DEVELASCO, R., AND LEDO, E. A.: *Hepatic abscess: clinical review of five cases.* (Arch. Hosp. Univers., Havana, 11, 4, 405-446).

During a ten year period, out of 1,000 cases reviewed, only 5 cases of liver abscess were found. The chief symptoms of diagnostic value were fever, pain in right hypochondrium, pain in shoulders, enlargement of liver, tenderness of the liver, and limitation of movement in the right pulmonary base. Probably infection is predisposed to by a long-standing state of lowered resistance in the liver itself. High leukocytosis is characteristic. Most cases are of amebic origin and, in all cases of undetermined etiology, emetine should be tried out. Medical treatment along with aspiration gives better results than open drainage. Chloroquine gives great promise in treatment and is less toxic than emetine, though emetine still holds first place in treatment. In the after-treatment of intestinal amebiasis, arsenicals should be avoided for fear of liver damage, and preference given to iodo-oxy-quinoleic derivatives.

NANSON, E. M.: *A new conception in the treatment of esophageal, gastric and duodenal lesions.* (New Zealand Med. J., April, 1949, Vol. 48, No. 264, 180-186).

The "new" conception which the author brings forth is simply the team work of the medical and surgical sections, with particular emphasis upon gastroscopy as a routine measure. The surgeon supervises all treatment, even though it be medical in nature, and thus there is a centralising of responsibility, which may be to the patient's advantage, especially if the surgeon conforms to the old definition of "a physician who knows how to operate."

COULTER, E. B.: *Traumatic diaphragmatic hernia with strangulation of stomach.* (Northwest Med., 49, 4, 267-268).

Coulter presents a case of traumatic diaphragmatic hernia which gave rise to acute symptoms one month following an automobile accident. Diagnosis was assisted by x-ray films. Operation by thoraco-abdominal approach revealed a massive herniation of stomach, small bowel, colon, left lobe of the liver and spleen. Strangulation had occurred and given rise to vomiting, pain and extreme dyspnea. The viscera were returned to the abdomen and a rent 3" x 3" in the diaphragm sewed up with silk ligatures. He made an uneventful recovery

LEWIS, A. E.: *Leiomyosarcoma of rectum: report of case.* (Northwest Med., 49, 4, 272).

Leiomyosareoma of rectum is rare. The present case occurred in a man 71 years old who complained of weight in the rectum, pressure on bladder, dysuria and increasing constipation over a period of several months. The tumor which was half as large as a lemon was low in the rectum and easily removed.

BAKER, J. S.: *Post-cholecystectomy symptoms.* (Bull. Mason Clin., June 1949, Vol. III, No. II, 1-8).

The most common causes of post-operative colic, following removal of the gall bladder are overlooked common duct or liver stones, overlooked dysfunction of the common duct or sphincter of Oddi (i.e., the dyskinesias), and residual inflammation in the biliary tract, liver or pancreas. The pain may have no relation to the biliary tract and result from incarcerated hiatus hernia, peptic ulcer or mesenteric adenitis. This last group of causes should be suspected when cholecystectomy was performed in the absence of stones. A single non-functioning cholecystogram is not enough to incriminate a gallbladder in which stones are not demonstrated.

BRICK, I. B. AND HORSTMAN, H. A.: *Liver biopsy.* (Bull. U. S. Army Med. Dept., Vol. IX, No. 8, 668-678).

This article is partly a general description of the value of liver biopsy in diagnosis and partly a description of cases of various kinds in which biopsy proved useful. The authors give vit. K for several days before needle biopsy. They insert the needle below the costal margin in cases where the liver is much enlarged, otherwise they use the 9th or 10th interspace in the mid- or anterior axillary line. Not only in hepatic diseases as ordinarily recognized, but in infectious mononeucleosis, acute brucellosis, sarcoidosis, pellagra, hemachromatosis and the exo-erythrocyte phase of malaria, liver biopsy is valuable. Serial liver biopsies form a valuable method of following the effects of treatment.

KRAFT, A., AND WOLF, W.: *Cholecystectomy.* Illinois M. J., 96, 4, 249-252.

A series of 210 operated cases of gallbladder disease were reviewed. On the whole, better postoperative results were obtained in cases in which stones were present and removed. The authors feel that the so-called "post-cholecystectomy syndrome" is a blanket term which actually covers a number of conditions, such as stones which failed to show in x-ray films, infected and dilated remnants of the cystic duct, incomplete stricture of the common duct, and also multiple adhesions involving the duodenum and liver. It is to be noted that they do not involve chronic hepatitis in this syndrome.

STRONG, G. F., PITTS, H. H., AND MCPHEE, J. G.: *Primary carcinoma of the liver—25 year study.* (Ann. Int. Med., Apr. 1949, Vol. 30, No. 4, 791-798).

Among 55 cases of proved, primary cancer of the liver seen at the Vancouver General Hospital in the past 25 years, 35 occurred in Chinese males, 2 in Japanese males, and 17 in white males and one white female. Forty-one of the cases were hepatomas and 14 cholangiomas. In almost every case, hepatic cirrhosis was present. The relation of the liver fluke to chronic liver disease including primary cancer deserves consideration, as the Chinese seen by the authors have, or have had, a high incidence of infestation with intestinal parasites, and the fluke was found in 4 of the Chinese males at autopsy. The course of the disease is rapid and resembles severe cirrhosis, with ascites, hepatomegaly, and sometimes splenomegaly. A negative x-ray report on a G. I. series is of some value in diagnosis. A hypochromic, normocytic anemia always was present. It is now possible to make an ante mortem diagnosis with reasonable accuracy.

KUMPURIS, F. G.: *Differential diagnosis of jaundice,* (J. Arkansas Med. Soc., April, 1949, Vol. 45, No. 11, 217-228).

This paper has the advantage of frankly admitting the difficulties in the medical, pre-operative diagnosis of jaundice. The author discusses the eleven liver function tests that he most greatly values in the differentiation between obstruction and hepato-cellular disease, but indicates, for example, that in obstruction, we may have definite liver disease as a complication or an association. The history of the case is of great importance in making a decision. Needle biopsy may prove valuable in following the course of a case. There is always a residue of cases in which diagnosis remains impossible and in these instances, surgical intervention is required.

KOWALEWSKI, K. AND FRANKEN, L.: *A case of hepatitis with marked hypercholesterolemia and hyperlipoidemia.* (Acta G. E. Belgica, Jan. 1949, Vol. XII, No. 1, 61-65).

In a case of hepatitis of toxic origin, with jaundice, although no xanthomatous lesions appeared, the highest value of cholesterol was 7.8 grams percent and of lipoids, 34.3 grams percent. After recovery from the hepatitis, the cholesterol value fell to 3.5 grams percent and the lipoids to 13.7 grams percent.

MONICA, A., GODINO AND FERREIRA, ANTONIO E. MENDES. *Multiple primary carcinomas of the large intestine and a Krukenberg tumor. (Carcinomas multiplos primarios do intestino grosso e tumor de Krukenberg).* Gaz. Med. Portuguesa 4, 2, 285. 1951.

The authors present a case of a patient who had a cancer of the rectum, which was removed by abdominal perineal resection. Twenty-two months later, the patient had two additional adenocarcinomas of the transverse colon without local recurrency or any sign of metastasis. Resection of the colon with end to end anastomosis was performed this time. One year following the second operation, the patient had another carcinoma of the ovarians, which was removed by bilateral oophoro-salpingectomy and hysterectomy. The last localization of cancer is considered as a Krukenberg tumor from the carcinomas of the transverse colon.

Franz J. Lust.

HOLTEN, C. AND LUNDBAEK, K. *Metabolic and renal diabetes following the administration of ACTH,* Scandinavian J. Clin. Labor. Investig. 2, 4, 317. 1951.

Determinations of blood sugar and urine sugar under standardized ingestion of food in two patients suffering from spondylarthritis ankylopoetica showed that during the administration of ACTH in doses varying from 60 to 100 mg. daily there appeared a delayed fall of the blood sugar after administration of carbohydrates, and a glucosuria without any rise of fasting or maximum blood sugar values. It seems as if ACTH causes both a metabolic and a renal diabetes. Examinations of the content of glutathione in the blood under the influence of ACTH gave no unequivocal results.

Franz J. Lust.

HANNAN, J. R., HAZARD, J. B. AND WISE, R. E.: *Carcinoid of the duodenum.* Am. J. Roentgen. & Rad. Ther., 66, 4, Oct. 1951, 569-76.

The authors present 3 cases of carcinoid of the duodenum. All showed a rounded filling defect in the duodenal bulb indistinguishable from benign tumors. Pathologically they were invasive. All were locally excised by transduodenal operation. The pathological and x-ray features of these tumors is discussed at length.

BOICE, C. L.: *Gastroileostomy: case report.* Am. J. Roentgen. & Rad. Ther., 66, 4, Oct., 1951, 601-602.

Boice describes a case in whom a gastroileostomy had been erroneously performed. The condition was surgically corrected by doing a gastric resection (Polya). The usual symptoms are nausea, vomiting, weight loss, pain and diarrhea. Diagnosis requires expert x-ray studies of the stomach and intestine. In this case a very small opening existed between the stomach and terminal ileum.

BROWN, G.: *Results of subtotal gastrectomy for peptic ulcer: a review of 60 cases.* Med J. Australia, Aug. 11, 1951, 185-187.

Although the author does not state how many of his cases were gastric and how many duodenal (and perhaps it doesn't matter) he obtained excellent results with only one death (coronary occlusion on the 7th post-operative day) and with comparatively few post-operative complaints. Two cases had really troublesome regurgitation, controlled by resting 30 minutes after meals. He had no cases of "dumping" and no cases of anemia of any type. He feels that radical resection of the stomach is indicated in pyloric obstruction, penetrating ulcer, and recurrent or severe hemorrhage.

IMAIZUMI, K.: *Clinical investigation of malaria psychosis.* Shikoku Acta Med., 1, 2, Dec. 1950, 93-99.

In New Guinea during the war, from 1943 to 1944, the author at a base hospital observed 143 cases of mental disease which included 93 cases of malarial psychosis. They were classified as delirium, "twilight state," amentia, coma, stupor, epileptic convulsions, Korsakow's syndrome, schizophrenia, manic state, "reactive state" and organic dementia. Delirium and schizophrenia were the commonest forms. It was characteristic of the manic state in malarial psychosis that abnormal emotions were less pronounced than in ordinary manic psychosis and clouding of consciousness was slight. In manic cases more tertian fever was found than in the other patients but no real relation existed between symptoms and the type of malaria.

NOACK, C. H. AND TRAUTNER, E. M.: *The lithium treatment of maniacal psychosis.* Med. J. Australia, Aug. 18, 1951, 219-222.

In spite of the well-known dangers of lithium poisoning, the authors have used lithium carbonate 0.6 gm. t.i.d.p.c. or lithium citrate 1.2 gm. t.i.d.p.c. with excellent results in manic patients. It was useless in schizophrenia. Toxic symptoms may occur about the 3rd or 4th day and include anorexia, nausea, vomiting and diarrhea, muscular weakness and uncertain gait, fasciculation of the muscles of the face, tremor, slurred speech, blurred vision, dizziness, vertigo and sometimes circulatory collapse. Massive doses of 1 to 2 percent Sodium chloride solution act as a prompt and effective antidote. In none of their cases was any instance of serious lithium intoxication encountered and it was never necessary to use sodium chloride. They treated 30 patients with mania by lithium during the past 2 years. Only one patient failed to respond. Nevertheless the authors recognize that lithium treatment may be dangerous and advocate further study in order to better select suitable cases for this therapy.

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INSTITUTE HEADS CITED BY N. Y. A. S.

New York, N. Y.—The New York Academy of Sciences, fourth oldest scientific society in the United States, has elected Dr. Maurice L. Tainter, Director of Sterling-Winthrop Research Institute, as a Councilor for 1952-54. The Academy has also elected Dr. C. M. Suter, associate director of the research institute, to fellowship.

The New York Academy of Sciences was organized in 1817, and its present membership is located in all 48 states as well as in 40 foreign countries.

BLAKISTON ANNOUNCES AGENCY APPOINTMENT

The Blakiston Company of Philadelphia, well-known publishers of medical and scientific books, announces the appointment of L. W. Frohlich and Company, New York, as the company's advertising agency, effective January 1, 1952. Campaign plans include direct mail and journal advertising. The announcement was made by Mr. T. A. Phillips, Editor-in-Chief and Vice President.

The Blakiston Company's line of books for under-graduate, graduate and professional schools, includes those in the fields of medicine, dentistry, pharmacy, chemistry, physics, zoology and the biological sciences—botany, horticulture and agriculture.

One of Blakiston's best-selling books is the "New Gould Medical Dictionary." The only new medical dictionary in 38 years, the "Gould" combines modern lexicographic methods with the most authoritative reference material. A unique feature of the "Gould" is the periodically published supplements which are supplied without charge.

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d-Alpha Tocopheryl Acetate (from vegetable oils) equivalent by biological assay to 2 International units of Vitamin E.

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Uses and Advantages: The water-soluble vitamins are available in separate layers on the outer part of the tablet; the fat-soluble vitamins are contained in the inner core, surrounded by an enteric coating. The water-soluble vitamins are released in the stomach and the fat-soluble vitamins in the small intestines so all vitamins are available at site of maximum absorption. Burping, regurgitation, fish taste or smell, and gastric disturbances are entirely avoided. Indicated as a daily dietary adjunct in children and adults; during pregnancy, to offset dietary restrictions, wherever vitamin supplementation is needed.

Administration: one or more tablets daily as needed.

Supplied: PANOVEMS—bottles of 50, 100, 250 and 1000 tablets.

PABALATE

Pabalate, a combination of sodium salicylate and sodium para-aminobenzoate prepared by the A. H. Robins Company, Inc., has been used with notable success in the treatment of rheumatoid arthritis and other rheumatic conditions.

Dr. Harry Beckman, Editor of the Year Book of Drug Therapy, has abstracted an article on this subject by Dr. Richard T. Smith, in the current (1950) issue of the Year Book. Dr. Smith's paper, *"Treatment of Rheumatoid Arthritis and Other Rheumatic Conditions with Salicylate and Para-aminobenzoic Acid: Study of 125 Patients,"* states that each patient was given sodium salicylate, 0.6-1.3 Gm., every four hours during the day for seven days. The dose was that which gave relief from pain and stiffness without producing serious toxic symptoms.

On the eighth day, this dose was replaced by 1 Pabalate tablet (5 gr. each of sodium salicylate and sodium para-aminobenzoate), and on the thirteenth day, the dose was increased to two tablets every four hours and continued until the twenty-first day.

Only 68 per cent of the patients experienced relief when taking the doses of sodium salicylate, while 92 per cent had equal relief when taking Pabalate, the abstract reported. Seventy-two per cent of the patients taking the sodium salicylate felt a need for additional medicine before the time for the next dose, but only two per cent reported this need when using Pabalate.

When patients were asked to estimate the degree of pain relief from the two types of medication, they agreed that there was distinctly greater relief from the Pabalate.

"Twenty-four hour pain relief can be achieved with Pabalate by proper repetition of dosage," reported Dr. Smith. This superiority of Pabalate was particularly noticeable in patients with rheumatoid arthritis or fibrositis.

Dr. Smith's paper reported a further significant point: When salicylate alone was taken, 55.2 of the patients showed certain toxic symptoms. However, when Pabalate was substituted, these symptoms disappeared entirely.

ADVANCE ORDERS

Advance orders for the new Sixth Edition of *The Merck Index, an Encyclopedia of Chemicals and Drugs,* scheduled for publication early in February, 1952, indicate that the first printing of 50,000

copies will be exhausted before publication.

The completely up-to-date Sixth Edition, published by MERCK & CO., Inc., manufacturing chemists of Rahway, N. J., contains 1,167 pages of text covering more than 8,000 descriptions of individual substances, more than 2,000 structural formulas, and about 20,000 names of chemicals and drugs alphabetically arranged and cross-indexed.

The special prepublication prices in the United States are $7.00 for the regular edition and $7.50 for the thumb-index edition. After publication, prices will be $7.50 and $8.00, respectively. Orders should be addressed to Publications Department, MERCK & CO., Inc., Rahway, N. J.

The previous edition of The Merck Index was published in 1940, and 60,000 copies were sold before the supply was exhausted during World War II. The new edition including extensive scientific advances since that time has been awaited by large numbers of chemists, pharmacists, physicians, dentists, veterinarians, botanists, and members of allied professions for whom the Index is an invaluable and unique reference work.

New features of the Sixth Edition include a table of standard buffers for calibrating pH measurements; a table of radioactive isotopes giving their half lives and type of radiation; and a table of current medical uses for radioactive elements and compounds.

A new section lists more than 300 organic "Name" reactions with original and review references, together with a description and structural representation of each reaction. There is an up-to-date periodic table, a table of international atomic weights, and close to 150 pages of appendices on such subjects as coal-tar colors, thermometric equivalents, anti-freeze mixtures, refractive index of liquids, saturated solutions, percentage solution tables for apothecaries, and atomic weights and their multiples and logs.

First edition of this comprehensive reference work was published in 1889, as "Merck's Index of Fine Chemicals and Drugs for the Materia Medica and the Arts—Comprising a Summary of Whatever Chemical Products Are Today Adjudged As Being Useful In Either Medicine or Technology." Subsequent editions before 1940 were published in 1896, 1907 and 1930.

Publication of The Merck Index, The Merck Manual of Diagnosis and Therapy, and The Merck Report, a quarterly journal in the interests of pharmacy and medicine, has become a traditional service rendered to the professions by Merck for more than half a century, during which time these three publications have achieved international recognition as dependable sources of information in the several fields which they are intended to serve.

(The accompanying notes on the new Sixth Edition of the Merck Index are from an article in the October issue of The Merck Report.)

NEW COMPANY IS FORMED TO CONDUCT CANADIAN PHARMACEUTICAL BUSINESS

Formation of Winthrop-Stearns of Canada, Ltd. to conduct the pharmaceutical manufacturing business of the Canadian branch of Winthrop-Stearns Inc., New York, was announced recently by Dr. Theodore G. Klumpp, president of the American firm and chairman of the board of the new company.

Charles B. McDermott has been named president of Winthrop-Stearns of Canada, Ltd., whose plants and general offices are located in Windsor, Ont. Associated with Winthrop-Stearns since 1926, Mr. McDermott has been general manager of its Canadian operation since 1947. He is a graduate of the University of Illinois who rose from professional service representative of Winthrop-Stearns in the United States to associate director of medical research of that organization and director of medical research of Winthrop Products Inc., which serves Latin-America, before being transferred to Canada.

Other officers of Winthrop-Stearns of Canada, Ltd. include Thomas R. Rider, vice president and sales manager; Henry L. Schade, vice-president; H. C. Eastman, secretary, and Percy Hawkes, assistant secretary. Mr. Schade is also president of Sterling Drug (Canadian) Limited.

Dr. Klumpp pointed out that "Winthrop-Stearns has operated in Canada through its branch for many years. The growth of the business in the Dominion now justifies changing the status of that operation from that of a branch to that of a corporate entity, namely, Winthrop-Stearns of Canada, Ltd.

"The manufacturing and distribution facilities of Winthrop-Stearns of Canada, Ltd. will be strengthened so that the new company may better serve the medical profession, the drug trade and the public in the Dominion. In addition, it will have available to it all the research facilities of Sterling-Winthrop Research Institute at Rensselaer, N. Y., and will expand its own research program in the light of Canadian needs."

The new company will continue the close and mutually beneficial relationship with Winthrop-Stearns Inc. Its products are manufactured at 1019 Elliot Street, Windsor, and its administrative offices are at 443 Sandwich Street.

MARCH OF DIMES

Research and teaching institutions throughout the United States and Canada have just been awarded over a million and three-quarter dollars in March of Dimes funds for further polio studies and professional education, it was announced today by the National Foundation for Infantile Paralysis.

$1,775,393 in March of Dimes funds will go to twenty-three medical schools, hospitals and research institutions in this country and one in Canada. The recent action by the National Foundation brings to approximately twenty-nine million dollars the amount provided since 1938 by the March of Dimes for furthering a search for a polio preventive and for the training of professional personnel. In addition, the organization has spent more than one-hundred-twenty million dollars for patient care during those years.

For investigations dealing with virus research, grants were made to:

The Children's Hospital, Boston, Massachusetts, $26,525, under the direction of Dr. John F. Enders, Chief, Research Division of Infectious Diseases.

University of Pittsburgh, Pittsburgh, Pennsylvania, $192,920,

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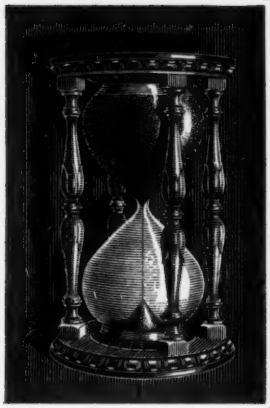

Prompt action—that is what patients like about Sal Hepatica. When Sal Hepatica is used, there is no laxative lag, no feeling of discomfort that persists for hours when slower-acting laxatives are taken.

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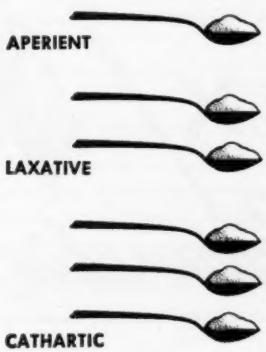
And the dosage is flexible. It may be adjusted to fit the need of the individual. A cathartic, laxative or aperient effect may be achieved by a simple regulation of the amount prescribed.



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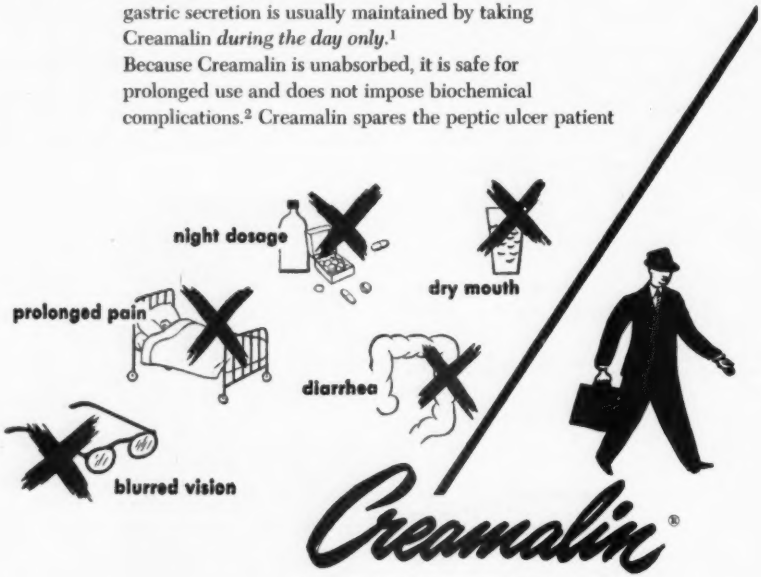
Creamalin heals peptic ulcer as quickly as 7 to 10 days. A reactive, demulcent type of gel, it buffers acidity for prolonged periods. Around the clock control of gastric secretion is usually maintained by taking Creamalin *during the day only.*[1] Because Creamalin is unabsorbed, it is safe for prolonged use and does not impose biochemical complications.[2] Creamalin spares the peptic ulcer patient



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1. Breuhaus, H. C., Akre, O. H., and Everly, J. B.: *Gastroenterology,* 16:172, Sept., 1950.
2. Jordan, Sara M.: ***Ann. West. Med. & Surg.,*** 4:133, Mar., 1950.

"Let's Get Down to Cases . . . "

"Although in experimental ulcers both the acid factor and the mucosal resistance factor are concerned, we have examples in which the acid factor predominates and others in which a decrease in the defensive properties of the mucosa predominates."*

*Peptic Ulcer. A. C. Ivy, M. I. Grossman and W. H. Bachrach, Blakiston Publishing Co., Phila., 1950.

Comprehensive therapy—whole duodenal substance, VIODENUM—provides an effective natural antacid plus factors which stimulate the mechanisms of repair and defense.

"Viodenum . . . increased the total volume of gastric secretion . . ." yet "Viodenum decreased the free acid . . ."*

*S. Krasnow, F. Steigmann and L. L. Hardt, Comparison of Effectiveness of Various Antacids on Gastric Acidity. Am. J. Dig. Dis., *17*:242 (1950).

peptic ulcer

Dr. P. J. Raimondi treated 59 proven cases of duodenal ulcer with Viodenum. He states, "A decrease in the annual rate of recurrence of symptoms was observed in patients with the highest frequency of exacerbations prior to treatment."*

*P. J. Raimondi, Treatment of Duodenal Ulcers with Desiccated, Defatted Duodenal Powder. Permanente Foundation Med. Bull., 8:4 (October), 1950.

Dr. Garnett Cheney treated 30 cases of ulcerative colitis. He states that Viodenum offers "... great promise in effecting a complete remission and possibly even a clinical cure . . . whole duodenal substance or Viodenum apparently promotes healing of the bowel by supplying some anti-ulcer factor . . ."*

*Medical Management of Gastrointestinal Disorders. Garnett Cheney, Yearbook Publishers, 1950.

ulcerative colitis

"Duodenal substance (Viodenum) was administered to 35 patients . . . the results obtained in 85% of the patients were very favorable . . . Viodenum may be considered a very valuable aid in the therapy of chronic ulcerative colitis."*

*M. H. Streicher, J. Lab. Clin. Med. *33*, 1633 (1948).

Viodenum, *the comprehensive approach:*

1. **Provides an effective natural antacid.**
2. **Provides factors which stimulate the mechanisms of repair and defense.**
3. **Provides natural mucin to soothe and protect irritated mucosa.**
4. **Stimulates gastric secretion yet decreases the free acid.**

Whole duodenal substance desiccated and defatted at body temperature.
Available in powder or ten grain tablets.

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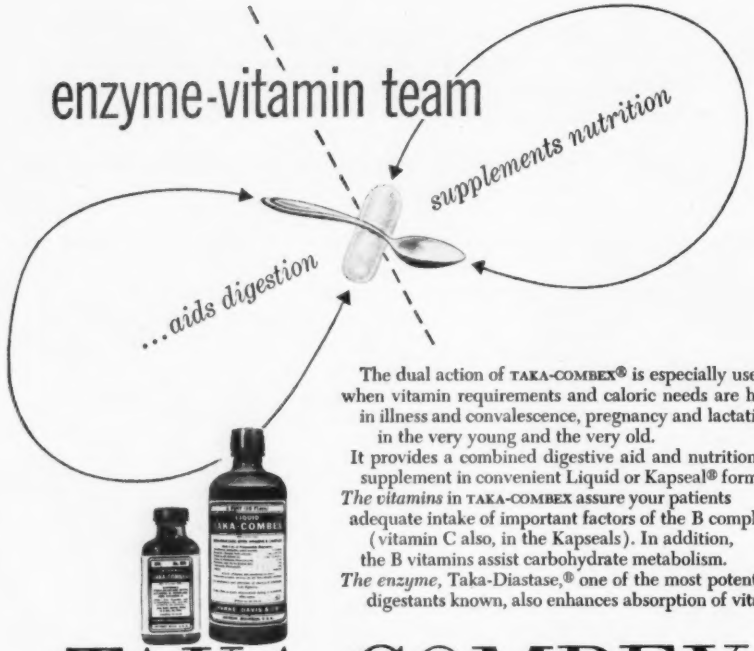

The dual action of TAKA-COMBEX® is especially useful when vitamin requirements and caloric needs are high—in illness and convalescence, pregnancy and lactation, in the very young and the very old.

It provides a combined digestive aid and nutritional supplement in convenient Liquid or Kapseal® form.

The vitamins in TAKA-COMBEX assure your patients adequate intake of important factors of the B complex (vitamin C also, in the Kapseals). In addition, the B vitamins assist carbohydrate metabolism.

The enzyme, Taka-Diastase,® one of the most potent starch digestants known, also enhances absorption of vitamin B.

TAKA-COMBEX Liquid Kapseals

TAKA-COMBEX Kapseals

Each Kapseal contains:

Taka-Diastase (*Aspergillus oryzae* enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	10 mg.
Vitamin B_2 (Riboflavin)	10 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (Sodium Salt)	3 mg.
Nicotinamide (Niacinamide)	10 mg.
Vitamin C (Ascorbic Acid)	30 mg.

With other components of the Vitamin B Complex derived from liver.
In bottles of 100 and 1000.

TAKA-COMBEX Liquid

Each teaspoonful (4 cc.) contains:

Taka-Diastase (*Aspergillus oryzae* enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	2 mg.
Vitamin B_2 (Riboflavin)	1 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (As the Sodium Salt)	2 mg.
Nicotinamide (Niacinamide)	5 mg.

In 16 ounce bottles.

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"The initiation of a healing reaction in the lesion is the surest safeguard against further bleeding"[1]

When therapeutic response must be prompt—the double gel action of Amphojel provides:

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- Protective coating of the exposed lesion to facilitate healing
- Quick relief of ulcer pain with subsequent release of mental and physical tension

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ALUMINUM HYDROXIDE GEL
ALUMINA GEL WYETH

Pleasant tasting . . . Economical
Available in bottles of 12 fl. oz.

1. Larimore, J. W.: Southern M. J. *44*:742, 1951.

Wyeth Incorporated, Philadelphia 2, Pa.

under the direction of Dr. Jonas E. Salk, Research Professor of Bacteriology.

University of Cincinnati—The Children's Hospital Research Foundation, Cincinnati, Ohio, $86,300, under the direction of Albert B. Sabin, Professor of Research Pediatrics.

University of Toronto—Connaught Medical Research Laboratories, Toronto, Canada, $54,850, under the direction of Dr. Andrew J. Rhodes, Professor of Virus Infections.

University of Wisconsin, Madison, Wisconsin, $8,110, under the direction of Dr. A. F. Rasmussen, Professor of Medical Microbiology and Preventive Medicine.

University of Utah, Salt Lake City, Utah, $54,190, under the direction of Dr. Louis P. Gebhardt, Professor of Bacteriology.

University of Michigan, Ann Arbor, Michigan, $105,000, under the direction of Dr. Thomas Francis, Jr., Professor of Epidemiology.

Stanford University, San Francisco, California, $17,710, under the direction of Dr. John A. Anderson, Professor of Pediatrics.

Tulane University, New Orleans, Louisiana, $10,045, under the direction of Dr. John P. Fox, Professor of Epidemiology.

Foundation of Applied Research, San Antonio, Texas, $11,075, under the direction of Dr. Nicholas T. Werthessen, Chairman, Department of Physiology and Biochemistry.

Western Reserve University, Cleveland, Ohio, $27,675, under the direction of Dr. Lester O. Kramptiz, Professor of Microbiology.

Western Reserve University, Cleveland, Ohio, $27,370, under the direction of Dr. Normand L. Hoerr, Professor of Anatomy.

New York University—Bellevue Medical Center, New York, New York $19,570, under the direction of Dr. Colin M. MacLeod, Professor of Microbiology.

University of Colorado, Denver, Colorado, $19,075, under the direction of Dr. Theodore T. Puck, Professor of Biophysics.

The Johns Hopkins University, Baltimore, Maryland, $5,325, under the direction of Dr. Roger M. Herriott, Professor of Biochemistry.

California Institute of Technology, Pasadena, California, $16,920, under the direction of Dr. Max Delbruck, Professor of Biology.

California Institute of Technology, Pasadena, California, $10,000, under the direction of Dr. Linus Paulding, Professor of Chemistry.

The University of Chicago, Chicago, Illinois, $38,100, under the direction of Dr. Earl A. Evans, Jr., Professor of Biochemistry.

Western Reserve University, Cleveland, Ohio, $13,725, under the direction of Dr. Harland G. Wood, Professor of Biochemistry.

Tulane University, New Orleans, Louisiana, $6,800 under the direction of Dr. Edwin D. Kilbourne, Associate Professor of Medicine.

For research seeking improved methods of treatment the following grants were approved:

Columbia University, New York, New York, $19,850, under the direction of Dr. Alvan L. Barach, Associate Professor of Clinical Medicine.

University of Colorado, Denver, Colorado, $6,975, under the direction of Dr. James J. Waring, Professor of Medicine.

Massachusetts General Hospital, Boston, Massachusetts, $3,245, under the direction of Dr. Joseph S. Barr, Professor of Orthopedic Surgery.

University of Nebraska, Omaha, Nebraska, $14,040, under the direction of Dr. A. R. McIntyre, Professor of Physiology and Pharmacology.

To increase the numbers of skilled professional persons required in carrying on research and in providing adequate care for patients, these awards were made:

American Academy of Pediatrics, Chicago, Illinois, $10,000, under the direction of Dr. E. H. Christopherson, Executive Secretary.

New York University College of Medicine, New York, New York, $21,006, under the direction of Dr. Howard A. Rusk, Professor and Chairman, Department of Physical Medicine and Rehabilitation.

Committee on Careers in Nursing, New York, New York, $27,392.59, under the direction of Miss Theresa I. Lynch, Chairman.

University of Washington, Seattle, Washington, $9,410, under the direction of Lillian B. Patterson, Dean of the School of Nursing.

Georgia Warm Springs Foundation, Warm Springs, Georgia, $14,490 under the direction of Dr. Robert L. Bennett, Director of Physical Medicine.

In addition, approximately $400,000 was appropriated to expand the professional scholarship and fellowship programs in the fields of medicine and the related biological and physical sciences, public health for physicians, physical therapy and medical social work. These awards are administered at National Foundation headquarters and are made upon the recommendation of committees from each of the professions concerned.

Included in this amount are funds for fellowships for Negro physicians to be administered by Provident Medical Associates of Chicago.

The announcement of the March of Dimes grants also disclosed that the National Foundation will continue to pay its share of the indirect costs of research. The Board of Trustees has approved approximately $300,000 for paying "a justifiable portion of the indirect costs of research which are not reflected in the usual budget of a research project." These costs include heat, power and light, building maintenance, and other similar operating charges which are not directly related to the research but which nevertheless drain funds from the university.

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NEW... finger-tip therapy

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Dihydrostreptomycin SULFATE SOLUTION

ready for use...

without reconstitution
without refrigeration

From drain-clear, silicone coated vials, each drop of Crystalline Dihydrostreptomycin Sulfate Solution freely flows through a 22-gauge needle—at a touch of your finger tips.

This new preparation, derived from pure Crystalline Dihydrostreptomycin Sulfate, presents the ultimate in easy "syringeability": it is immediately ready for use—injection procedure is rapid and virtually effortless.

Each 2 cc. provides the equivalent of 1.0 Gm. of pure dihydrostreptomycin base.

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in two convenient sizes:

2 cc. vials, containing 1 Gm. dihydrostreptomycin in solution.

10 cc. vials, containing 5 Gm. dihydrostreptomycin in solution.

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in dry form for preparation of aqueous solutions for parenteral use:

Dihydrostreptomycin Sulfate and Streptomycin Sulfate: in bottles of 1 Gm. and 5 Gm.

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For use when oral administration is difficult or impractical—when more prompt action is desired.

Banthine—a true anticholinergic drug with an adequate range of safety—is now made available to the medical profession in parenteral form, for use intravenously or intramuscularly in those conditions characterized by nausea and vomiting, when oral medication cannot be retained and when a prompt action is desirable.

Through its anticholinergic effects, Banthine inhibits excess vagal stimulation and controls hypermotility.

In Peptic Ulcer—the value of the oral form of Banthine is now well established. However, edema in the ulcer area may indicate parenteral Banthine until the healing processes have reduced the edema.

In Pancreatitis—it has been found that parenteral Banthine relieves pain, effects a fall in blood amylase and produces a general improvement in the patient's condition.

In Visceral Spasm—it inhibits motility of the gastrointestinal and urinary tracts.

Parenteral BANTHĪNE is supplied in serum-type ampuls containing 50 mg. of Banthine powder. Adult dosage is generally the same as with Banthine tablets.

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